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RHEUMATISM

ITS NATURE PATHOLOGY AND TREATMENT

T. J. MACLAGAN

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RHEUMATISM

RHEUMATISM
ITS NATURE, ITS PATHOLOGY
AND
ITS SUCCESSFUL TREATMENT

BY

T. J. MACLAGAN, M.D.

PHYSICIAN IN ORDINARY TO THEIR ROYAL HIGHNESSES PRINCE AND
PRINCESS CHRISTIAN OF SCHLESWIG HOLSTEIN

SECOND EDITION

LONDON
ADAM AND CHARLES BLACK
1896

PREFACE TO THE SECOND EDITION

SINCE the opening sentences of the first preface were written twenty years have elapsed—a big gap in the lifetime of man. Many changes have taken place in the profession since then. Of those who were over fifty then, nearly all have passed away, and a new generation has replaced them. Of the changes which have taken place in the practice of medicine during these years there is none more striking than the change in the treatment of acute rheumatism. Those who have known that disease only under the salicyl treatment can have no idea of the hopeless dread with which one undertook the charge of rheumatic fever in the old days. It was the despair of physicians. For weeks it went on—the agonising pain, the sleepless nights, the drenching perspirations, the look of misery, the piteous appeals for relief, in response to which we had nothing to give but words of sympathy and encouragement, an occasional opiate, and “six weeks in bed.” It recurs to one now as a horrid nightmare.

Yet was it a very stern and very common reality. But all is changed. Rheumatic fever as it formerly existed is unknown to the present generation, and there is now no disease whose treatment the physician undertakes with more cheerful confidence, and with such a certainty of being able to effect a speedy cure. "I never see rheumatic fever now," said the late Dr. Wilson Fox to me once; "when a case comes into hospital the house-physician prescribes full doses of salicin or salicylate of soda, and the man is practically cured before I see him."

In the light of the experience acquired during these twenty years it may be well once more to go over the ground which we formerly traversed, and reconsider the whole subject of the pathogenesis of rheumatism and the mode of action of the salicyl compounds.

9 CADOGAN PLACE, LONDON,
May 1896.

PREFACE TO THE FIRST EDITION

“A PERUSAL of the literature which bears on the question of the treatment of acute rheumatism (rheumatic fever) is a task from which few would rise with any definite idea as to how that disease is best treated. Purgatives, diaphoretics, sedatives, alkalies and alkaline salts, colchicum, aconite, quinine, guaiacum, lemon juice, sulphur, mercury, veratria, tincture of muriate of iron, etc., would each be found to have in turn attracted the favourable notice of one or more of those who have directed attention to the subject. Of all these different remedies not one stands out prominently as that to which we can with confidence look for good results. We have, indeed, no remedy for acute rheumatism—a malady which not unfrequently proves fatal, which is always accompanied by great pain, and is a fruitful source of heart disease.

“Under these circumstances I need make no apology for bringing under the notice of the profession a remedy which, so far as my observations have gone,

has given better results than any which I have hitherto tried—and I have tried all the usual remedies over and over again.

“In the course of an investigation into the causation and pathology of acute febrile ailments, which has for some time engaged my attention, I was led to give some consideration to intermittent and to rheumatic fever. The more I studied these ailments, the more was I struck with the points of analogy which existed between them. On a detailed consideration of these I shall not now enter. Suffice it to say that they were sufficiently marked to lead me to regard rheumatic fever as being, in its pathology, more closely allied to intermittent fever than to any other disease, an opinion which further reflection and extended experience have served only to strengthen.”

Such are the opening sentences of the paper in which, in March 1876, I introduced salicin to the notice of the profession as a remedy in acute rheumatism.

In this volume the miasmatic theory of rheumatism, there referred to, is expounded; and an explanation offered of the manner in which the salicyl compounds produce the marked anti-rheumatic effects which they are now all but universally acknowledged to possess.

The plates representing the early changes noted on the surface of the endocardium in cases of rheumatic endocarditis, are taken from Dr. Green's *Introduction to Pathology and Morbid Anatomy*. For permission to use them I have to thank Dr. Green and his publisher.

9 CADOGAN PLACE, LONDON, S.W.,
May 6, 1881.

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ON RHEUMATISM

CHAPTER I

THE VARIETIES AND SYMPTOMS OF RHEUMATISM

RHEUMATISM is generally described as occurring in three forms—the acute, the subacute, and the chronic. For clinical purposes this is as convenient a classification as can be given.

ACUTE RHEUMATISM or rheumatic fever generally commences with a feeling of cold and malaise, followed by a sense of weakness, and aching pains in the neck, back, and limbs. The pains increase in severity and are soon localised in one or more of the large joints, which become swollen and very tender.

The inflammation of the joints, which gives rise to the suffering of acute rheumatism, forms the most prominent and characteristic feature of the fully developed disease. As a rule, it is confined to the large joints; the knee, ankle, wrist, elbow, shoulder, and hip joints being attacked with a frequency which corresponds very

much to the order in which they are enumerated. Of the small joints those of the fingers are most apt to suffer. In striking contrast with what is observed in gout, the joints of the foot, other than the ankle, are rarely affected.

The local symptoms of the disease are pain, swelling, and great tenderness of the inflamed joints. Occasionally there is redness of the surface. But such redness is less marked and less common than in gout. The inflammation shows a marked tendency to shift from joint to joint. This alternation of pain and freedom from pain may be experienced by most of the large joints of the body during one attack of the disease. The invasion of fresh joints is not always accompanied by diminution of the inflammation in those already affected. But occasionally there is noted what seems to be, and is by many regarded as, a true metastasis—a retrocession of the inflammation from one joint to another.

Febrile symptoms are marked. The pulse and respirations are increased in frequency. The temperature varies from 100° to 104° Fahr., but has no distinctive range. The general course of the fever is irregular rather than continued. Just as the local joint affection is made up, not of one long continued attack, but of a succession of short ones, so the febrile symptoms consist, not of one long continuous seizure, but of a series of short ones, whose duration and severity correspond very much to the duration and severity of

the local inflammatory attacks. During the whole course of the ailment there is no time at which the patient is free from pain or fever ; but there may be many ups and downs in the course of both before the ailment comes finally to an end.

The skin is very active in acute rheumatism. The surface is usually bathed in a profuse perspiration, which is a source of much general discomfort. It has a sour disagreeable odour and an acid reaction. The naturally alkaline saliva may also be acid.

The urine is hyperacid, scanty, high-coloured, and on standing throws down a copious deposit of urates. Its specific gravity is high, and it contains an increased quantity of urea. The bowels are constipated. The tongue is coated with a thick white fur. The appetite is gone. There is considerable thirst.

The patient's condition in a severe case is pitiable in the extreme. He lies on his back unable to move, the least effort to do so causing intense pain. The perspiration trickles down his face, but he cannot wipe it away. Even the weight of the bed-clothes cannot be borne. He dreads the approach of his friends, screams with agony at the least touch, and sometimes even without such a cause. His expression is that of intense suffering and abject helplessness. He gets no rest. His one desire is to have some relief from pain. The disease varies in duration ; but, when uninfluenced by treatment, the acute symptoms generally last for two or three weeks.

During its course there is a marked tendency to inflammation of the structures of the heart. This constitutes the chief danger and anxiety of the illness ; for the heart, when once affected, is apt to be permanently damaged ; while in not a few cases the cardiac inflammation proves directly fatal in its acute stage.

The great majority of cases of acute rheumatism do recover. The prognosis, therefore, is favourable.

In some cases, fortunately in very few, the temperature runs up to 106° , 108° , or even 110° . With this high temperature there are associated alarming nervous symptoms. This constitutes that form of the disease to which, from its fatality, the term "malignant" has been applied ; but which is now generally described under the name of rheumatic hyperpyrexia.

SUBACUTE RHEUMATISM is a milder form of the same disease, and presents the same symptoms and features in a minor degree. It comes on more gradually, generally like an ordinary cold, and usually without any initial rigor. Fewer joints are affected at one time ; the inflammation of the individual joints is less severe ; the pain is less exquisite, and the swelling less marked. There is, however, some swelling, and very decided tenderness. The joint affection shows the same tendency to shift, and vary its seat ; but the patient is less helpless, and his general condition less

distressing. The perspiration is acid, but not so profuse. The heart is apt to suffer in this, as in the more acute form, but not quite so frequently; when it is affected the inflammatory action partakes of the generally milder character of the ailment, and is more rarely a source of immediate danger. The remote consequences are apt to be the same in both. The temperature ranges from 99° to 101° . Well-marked cases of subacute rheumatism run by insensible gradations into mild cases of the acute form of the disease.

CHRONIC RHEUMATISM is a name which is loosely applied to many ailments not really of rheumatic origin. Almost any obscure and obstinate pain which is not traceable to some other agency is apt to be attributed to chronic rheumatism. Under this head there thus come to be ranked many aches and ailments which, not being of rheumatic origin, have no claim to the title. Chronic rheumatism, properly so called, is a milder form of the subacute variety, in which there is not sufficient local inflammation to lay the patient up, or to raise the temperature.

Just as the acute runs into the subacute, so the subacute runs into the chronic by insensible gradations. It is sometimes the precursor, often the sequence, of an acute or subacute attack. It also exists independently of them. “Remarquons d’abord qu’à un degré très léger, et lorsqu’il n’occupe qu’un petit nombre d’articulations d’un volume peu considérable, le

rhumatisme articulaire est souvent apyrétique, à quelque période qu'on examine les malades.”¹

The malady is characterised by the occurrence of pains, obstinate in nature, and sometimes shifting in character, affecting the joints, muscles, and fibrous aponeuroses. The affected parts may be somewhat tender to touch, but are not, as a rule, distinctly swollen. The pain is increased by damp and cold. It often disappears in fine, and returns in wet weather. Unless the patient is in easy circumstances, he may never be confined to the house, and never consult a medical man; but may go about his daily work until he gets better, or until the onset of an acute or subacute attack compels him to lay up. It is a troublesome ailment which frequently lasts, off and on, for months. During its continuance there is often laid the foundation of future cardiac troubles. The temperature may now and then rise to 99°, or even a little higher—making the case for the time subacute; but generally it is normal. The pulse is not quickened.

In the age, in the personal and family history of the patient, in the seat of the pain, in its shifting character, and in the occasional slight rise of temperature, we have the best means of distinguishing true chronic rheumatism from the other ailments, gouty, arthritic, and neuralgic, with which it is so often confounded. It is of the utmost importance that such a distinction should be made, for on the accuracy of our diagnosis

¹ Bouillaud, *Traité Clinique du Rhumatisme Articulaire*.

depends our ability to relieve the patient, and mitigate his sufferings.

The diseases for which acute and subacute rheumatism are most apt to be mistaken are acute gout, acute rheumatoid arthritis, pyæmia, and gonorrhœal rheumatism. As a rule, the differential diagnosis presents no serious difficulty.

Acute gout is a disease of mature years; acute rheumatism a disease of youth. Gout generally affects only one joint, rheumatism several. Gout attacks chiefly the small joints, rheumatism the large. In acute gout the skin over the affected joint is red and glistening; in acute rheumatism, as a rule, redness of the surface is not marked. In acute gout the skin is dry and unperspiring; in acute rheumatism it perspires very freely. In acute gout the blood contains uric acid; in acute rheumatism it does not. Acute gout is not benefited by salicin and salicylic acid; acute rheumatism is speedily cured by them. Acute gout is much less apt to affect the heart.

Acute rheumatoid arthritis resembles subacute rather than acute rheumatism. It is distinguished from it by the following peculiarities:—Acute rheumatoid arthritis is a comparatively rare disease. It occurs chiefly among young women whose health has already been impaired by some debilitating cause, generally menstrual or uterine disturbance, or prolonged lactation. It comes on more gradually

than rheumatism. It attacks the small joints as frequently as the large. It shows no tendency to shift from joint to joint. The skin does not perspire profusely as in acute rheumatism. It is a more obstinate ailment, and does not yield to remedies which speedily cure rheumatism. It does not tend, like this, to affect the heart.

Pyæmia.—Cases of pyæmia sometimes occur in which the presence of joint inflammation, possibly also of endocardial inflammation, of febrile symptoms, and of free perspiration, give to the ailment some resemblance to a case of acute rheumatism.

The diagnosis is not difficult. In pyæmia there is the existence of some wound or other lesion to explain its occurrence; the rigors are more marked; the joint inflammation does not shift about; the perspiration is not acid; and the general symptoms are of a more markedly typhoid type. Should we fail to make a diagnosis by these means, the doubt is not unlikely to be soon set at rest, if the case be one of pyæmia, by the onset of alarming typhoid symptoms, and a speedily fatal result.

Gonorrhæal rheumatism occurs in connection with gonorrhœa. It is not accompanied by the same amount of febrile disturbance as acute or even subacute rheumatism. It affects fewer joints; has a special preference for the knee; and does not show the same tendency to shift about. Acid perspirations

do not occur; and it does not tend to affect the heart. Remedies which speedily cure true acute rheumatism have no influence on the gonorrhoeal form of the disease.

There is another morbid condition to which the term rheumatism is usually applied, but which is more properly a sequence of rheumatism than a distinct form of the disease, and which is so apt to be mistaken for the subacute and chronic forms of the malady, that it will be well to refer to it here.

When a man has suffered from repeated rheumatic attacks, especially when these have followed each other in quick succession, there is apt to be induced a state of chronic thickening of the fibrous textures involved in the disease. The nature of the change, and the influence exercised by it on subsequent rheumatic attacks, will be considered hereafter. Meantime, its existence is indicated with the object of pointing out that this condition, though of rheumatic origin, exists, when developed, independently of the rheumatic poison, and may give rise to symptoms indistinguishable from those caused by it—pain and stiffness of the joints. The importance of recognising its existence will be apparent when we come to consider the question of treatment.

Scarlatinal rheumatism. — In the course of scarlatina, generally during its desquamative stage, a form of arthritis is occasionally developed which so

closely resembles that of acute rheumatism that it has received the name of scarlatinal rheumatism. Scarlatinal arthritis would be a more correct name, for the disease is not caused by the rheumatic poison, but is a sequela of scarlatina, as it at times is of measles, of typhoid fever, and of parturition, and is no more of rheumatic origin than is the endocarditis or the pleuritis which may also occur at the same stage of scarlatina. Arthritis is one of the sequelæ of scarlatina.

We know from what is seen in gout, in rheumatoid arthritis, in pyæmia, in gonorrhœa, that poisons other than that of rheumatism may cause inflammatory changes in joints. One of these causes is the scarlatina poison, or some morbid agency brought into operation during the course of its action on the system.

CHAPTER II

THE DURATION OF RHEUMATISM

NEXT to pain and the heart complications, the most notable feature of rheumatism is its prolonged duration. That the chronic form should be thus characterised, is no more than one would expect in an ailment to which the term chronic is applicable. It is in connection with the acute and subacute forms that this feature calls for special notice. The long duration of acute rheumatism has been remarked by every one who has written on the subject. It is this which imparts to the ailment many of its horrors.

Till very recently it was no uncommon thing for the disease to last for months ; and only in exceptional cases did the patient have less than three weeks of suffering. "In my last attack, I was in constant agony for six weeks." "Every attack has laid me up for three or four months." Such, till within very recent years, were the common experiences of those subject to the disease. A considerable variety in the duration of different cases has always been noted as a leading feature in its natural history. Some are exceptionally

long; others exceptionally short. Hence the mean duration of the malady varies with the varying experience of different observers. But all agree in calculating this by weeks rather than by days.

Pinel says that it lasts from seven to sixty days.

Scudamore remarks that, "In a case of which the issue is favourable, the fever and pains are brought to a close at the end of the third week; and in slight attacks at an earlier period; but when the course of the disease is untoward, a period of two months scarcely serves to exhaust its power in producing even acute symptoms."

"How long," says Macleod, "a case of acute rheumatism of medium severity might endure, if left to itself, I am unable to say; but, with the common methods of treatment, probably five or six weeks may be about the average duration of rheumatic fever."

According to Chomel, the disease rarely disappears before the twentieth day, and is sometimes prolonged for three months.

Bouillaud states that, under the modes of treatment adopted up to the time at which he wrote (1840), the mean duration of acute rheumatism was forty to fifty days; but that, under the influence of the treatment to which he had recourse (bleeding *coup sur coup*), it was reduced to less than half that time, *i.e.* about three weeks.

Fuller says that his own observation led him to believe "that even when unattended by any internal affection, the disease, under ordinary methods of treatment, endures from four to five weeks."

Garrod puts it at "from ten days to three or four weeks."

Niemeyer gives the duration of mild cases as "one or two weeks"; and of severe ones as "many weeks."

Senator says that "as a rule acute polyarthritis runs its course in from three to six weeks."

Lebert gives the statistics of 108 cases, of which—

10	lasted from	5 to 15	days,
58	„	„	16 to 35 „
32	„	„	36 to 55 „ and
8	„	„	56 to 80 „

In Dr. Bristowe's work on *Practice of Medicine*, published in 1876, the duration of acute rheumatism is thus referred to: "There is no definite limit to the duration of acute rheumatism. Sometimes the patient recovers completely in the course of a day or two, or of a week; more commonly the disease persists for several weeks; and not unfrequently it becomes chronic, or is continued by successive relapses for a much longer period than that."

In the St. Thomas's Hospital reports for 1872, Dr. Peacock gives a statistical account of the cases treated in that hospital during the previous year. He there states that the largest proportion of cases

recovered in the fourth week. This may be accepted as consistent with general experience.

With regard to hospital statistics on this subject, however, it has to be remarked that the proportion of acute to subacute cases is larger in private than in hospital practice. The explanation of this is to be found in the difficulty, or even impossibility, of removing a very acute case to hospital during its very acute stage, and such cases are very acute from the commencement. Over and over again have I seen cases of subacute rheumatism brought into hospital with a history of acute rheumatism of several weeks' duration. The explanation of the delay in sending them generally was, that they were too ill to be moved. And one can quite see the force of that. A man who cannot bear the weight of the bed-clothes, who screams with agony at the least shake of his bed, or at the lightest touch of a friend, is one whom it would be impossible to subject to the movement and disturbance inseparable from conveyance to another locality. For this reason, very acute cases are more often seen in private than in hospital practice, and hospital statistics are to be regarded as giving to acute rheumatism a milder aspect and shorter duration than would be got from similar statistics taken from private practice. For the same reason, Dr. Peacock's statistics probably under- rather than over-state the mean duration of all cases of acute rheumatism.

Such are the statements of the best authorities. All agree in ascribing to acute rheumatism a mean duration of several weeks; and this consists with the experience of every practitioner. No one who saw much of the disease before the days of the salicyl treatment, can fail to recall, on the one hand, cases in which the patient, to the delight of himself and attendants, got over the attack in one or two weeks; and, on the other hand, cases which dragged on their weary and painful course for six or eight weeks, and even more.

The duration of the disease is determined by the duration of pain, its most prominent and characteristic feature. Pain, of course, is only one symptom, but it is that which is most characteristic, which is most complained of, which continues so long as the rheumatic poison exercises its action on the joints, and without which rheumatism cannot be said to exist. The temperature may decline, the pulse may fall, the perspirations may cease; but so long as pain remains in any of the joints, the patient is not convalescent, and may have a re-accession of all his symptoms.

Nowadays we have in the thermometer a delicate means of determining the duration of the febrile symptoms, which are an essential characteristic of acute rheumatism. It is found that the objective evidence thus got accords very closely with the subjective evidence derived from the patient's feelings,

on which our fathers relied. The temperature falls and rises with the decrease and increase of pain and swelling in the joints, but rarely comes permanently to the normal standard till the joint pain disappears. The cases in which the joint pains persist after the normal temperature has been reached, are those in which the chronic form of the disease follows in the wake of the acute, and in which this sequence of events imparts to the attack an unusually prolonged duration, if we calculate this by the duration of the pain alone.

This grafting of the chronic on to the acute or subacute form explains the long duration of those cases in which acute rheumatism is said to have lasted for several months. Such cases commence as acute rheumatism, gradually pass into subacute, and still more gradually into the chronic form. So insensible are the gradations by which the one form runs into the other that with the thermometer it is difficult, and without it impossible, to say exactly when acute becomes subacute, and subacute chronic. It is seldom, however, that a case remains acute for more than three weeks. It may be acute for that time, subacute for three or four weeks more; then gradually, and without cessation of pain, pass into the chronic form, and so remain for many weeks—the whole duration of the ailment being several months. It is one attack all through; but it is not *acute* rheumatism during its whole course.

The chronic course of such cases may be interrupted and varied by subacute exacerbations of longer or shorter duration, serving to show that the chronic form of the disease owns the same causation as the acute and subacute forms which precede and follow it.

These very prolonged cases are exceptional. Generally the febrile symptoms and the pain decline and disappear about the same time.

The authorities and statements which have been quoted, existed and were made before 1876, the year in which the salicyl compounds were introduced for the treatment of acute rheumatism. When we come to consider the duration of the malady under this treatment, it will be seen how vast are its benefits. For whereas this duration was formerly calculated by weeks, it is now estimated by days. Taking pain as the index of its continuance, it will be found that, when the salicyl treatment is properly applied, the disease lasts as many hours as it formerly did days; or as many days as it formerly did months. For, in many cases, the pain is now more effectually and surely relieved in one day than it formerly was in one month. The temperature, too, falls to the normal very soon after the pain is abolished.¹

¹ The late Dr. Wilson Fox once remarked to me, "I never see acute rheumatism now; as soon as a case is admitted to hospital, the house physician gives him salicin or salicylate of soda, and he is cured before I see him."

CHAPTER III

THE SEAT OF RHEUMATISM

THOUGH some difference of opinion is found among old authors as to the exact seat of rheumatism—Latham, for instance, regarding the lymphatics, and Carmichael Smyth the muscles, as being specially involved,—the malady is nowadays generally believed to have its seat chiefly in the fibrous and serous tissues.

And there is good reason for this belief. The rheumatic poison is found to exercise its action on, and almost exclusively on, particular organs and textures in which these tissues predominate, and which seem to have no other feature in common. The joints, muscles, and heart are the parts chiefly involved. In the case of the joints, it is not the osseous, but the fibrous and serous elements—the capsules, ligaments, tendons, and tendinous sheaths, and the synovial membranes—which suffer. So with the heart: the white fibrous structure of the rings and valves, and the serous investing membrane, suffer much more than the muscular substance.

Fibrous or serous tissue appears to be requisite to the action of the rheumatic poison, and to the development of rheumatism.

But all fibrous and serous textures are not equally apt to suffer. There are many joints which enjoy a comparative immunity from the disease. The small joints of the fingers are not often affected. The small joints of the toes more rarely still. True rheumatic inflammation of the articulation of the lower jaw, or of the joints of the atlas and axis is comparatively rare. And I never saw, or heard of, a case in which the articulations of the ribs were involved. And yet all these joints have ligaments, and fibrous and serous tissues. The fibrous membranes which surround the brain and spinal column; the fibrous membrane which covers the bones externally; and those which invest and give support to the liver, spleen, kidneys, and uterus, exceed in quantity the fibrous textures of the large joints and of the heart; and yet, for once that rheumatic inflammation occurs in any one of these membranes, it occurs many hundred times in the ligaments of the large joints.

The serous investing membranes of the brain, of the lungs, and of the abdominal organs, far exceed in extent the corresponding membrane of the heart; but for once that any of them is the seat of rheumatic inflammation, the pericardium suffers a hundred times.

In structure all white fibrous tissue is very much alike; but in function it varies much. The chief of its functions are—

(1) To support entire organs.

(2) To bind together and give support to their constituent parts.

(3) To control and regulate movement.

That which supports entire organs is instanced in the fibrous coverings and appendages of the liver, spleen, uterus, etc. That which binds together and gives support to their component textures is instanced in ordinary connective tissue. That which is engaged in controlling and regulating movement is exemplified in the fibrous textures of the joints. It is this last form of white fibrous tissue which is specially involved in rheumatism.

One of the chief functions of serous membrane is to facilitate movement. In some organs, which are provided with a serous investment, the movements are so slight that the membrane has no very active function to perform in this way. The only serous membranes actively engaged in such work are the investing membrane of the heart, and the lining or synovial membranes of the larger joints, which, in function, are to be regarded as serous membranes.

Now, putting these various facts together,—finding that many of the fibrous and serous tissues of the body are not subject to rheumatism, but that the disease is limited almost entirely to such fibrous and serous tissues as are habitually engaged in facilitating, regulating, and restraining active movement,—we cannot fail to see that the seat of rheumatism is not fibrous

tissue in general, but such fibrous tissue as is habitually engaged in controlling and regulating movement ; and not serous textures in general, but such serous textures as are habitually engaged in facilitating free and active movement.

In other words, rheumatism is essentially a disease of the motor apparatus, and the chief seats of the morbid process are the fibrous and serous structures of that apparatus.

There are fifteen common seats of rheumatic inflammation—two hips, two knees, two ankles, two shoulders, two elbows, two wrists, two hands, and one heart ; and the one functional characteristic common to the fibrous textures of all is that they are habitually engaged in controlling and regulating movement. They are the only fibrous textures which possess this function.

But though the fibrous structures and synovial membranes are the tissues on which the rheumatic poison produces the most marked effects, they are not the only ones which give evidence of disturbance. The evidence is most pronounced in them, because the symptoms which constitute it—pain and swelling—are so prominent and obvious. So much do such symptoms force themselves upon the notice of both patient and physician, and so dominant are they during the whole course of the disease, that attention is naturally concentrated on them. But a careful consideration of all the phenomena which go to con-

stitute an attack of acute rheumatism indicates that the muscles suffer at the same time as the joints. Their participation in the morbid process is indicated by the muscular pains and aching which usher in the attack, by the tenderness to touch of the muscles, and by the rapidity with which their tissue wastes away.

Further very distinct evidence of disturbance of the muscles is found in what, next to the joint pains, is the most essential and characteristic feature of the disease—excessive formation of lactic acid. This phenomenon calls for explanation as urgently as the joint inflammation, for it forms as characteristic and as constant a feature of acute rheumatism—acid sweats being almost as essential to the diagnosis of acute rheumatism as joint pains.

Lactic acid is a normal product of the metabolism of muscle. In its quiescent state muscle gives a neutral or feebly alkaline reaction; when actively contracting the reaction is acid. This acid reaction is due to the presence of lactic acid formed during the state of activity. Lactic acid being formed during muscle metabolism, excessive formation of that acid in the system indicates increased metabolism of muscle. As this excess of acid always occurs in acute rheumatism and never in any other disease, it follows that an increase in muscle metabolism is one of the characteristic features of the rheumatic process—one of the results of the action of the rheumatic poison. The consideration of the question of an

excess of lactic acid in the system really resolves itself into the consideration of the question as to why muscle metabolism is increased. To this point we shall return by and by. Attention is called to it now with the object of showing that the rheumatic process is not limited to the white fibrous structures of the joints, but affects all the fibrous structures of the motor apparatus—the muscles as well as the tendons and ligaments.

CHAPTER IV

THE NATURE OF RHEUMATISM

THE nature of the change which takes place as the result of the action of the rheumatic poison has been matter of some difference of opinion. The one point on which all are agreed is that it is inflammatory. The point on which opinions differ is as to the nature of the inflammation.

Rheumatic inflammation has been regarded by some as differing from ordinary inflammation, not essentially, but only in the peculiarity of its seat. By others it is looked upon as specific in nature, as resulting from the action of a special poison which does not operate in the production of other than rheumatic inflammation. The former is the view taken by those who regard the disease as the direct result of exposure to cold and damp; the latter that held by those who look upon it as due to the action of a special *materies morbi* circulating in the blood.

That exposure to cold and damp suffices to produce acute rheumatism is an old view which finds its chief

support in the fact that the disease often occurs after such exposure. But so frequent is such exposure, that it would be difficult to point out any disease which might not be attributed to this agency, if we are not careful to distinguish between the *post* and *propter hoc*.

If acute rheumatism owned such a causation, it ought to be most common in the coldest climates, and during the coldest weather. But it is a disease of temperate climates, not of the Arctic regions; and in temperate climates, is not always most common in winter.

It ought, too, if caused by cold, to be most common in children and in old people, who have little power of resisting cold; but the reverse is the fact; for the disease is most common at the age at which the power of resisting cold is greatest—from fifteen to fifty. If caused by exposure to cold, the joints which suffer most from such exposure, those of the fingers and toes, should also suffer most from rheumatism; but they are very rarely involved in the disease. Then, again, if this be the cause of the disease, how is it that pericarditis so frequently occurs, and pleuritis and peritonitis so rarely? The pleura and peritoneum are just as much exposed to cold as the pericardium, probably more so. And how, on this view, are we to explain the occurrence of endocarditis, and the almost entire limitation of this to the left side of the heart?

Again, it is an established fact in the history of

acute rheumatism, that fresh joints may be attacked after the sufferer has been confined to bed in a warm room for days and even weeks. These later joint attacks are identical in nature with the earlier ones which ushered in the seizure, and it would be unreasonable not to regard them as produced in the same way, and as due to the operation of the same cause. But it is quite impossible that they can be caused by exposure to cold. The exclusion of cold as a possible agency in the production of these later joint seizures is a sufficient reason for calling in question its claims to be the cause of the earlier ones.

Other peculiarities of acute rheumatism there are which it is impossible to explain on this view of its etiology. The mere enumeration of these will suffice to show that no amount of exposure is adequate to their explanation.

The special characteristics of acute rheumatic inflammation are—

(1) The tendency to its occurrence is hereditary—transmitted from father to son.

(2) It is specially liable to occur at a particular age—being rare before fifteen or after fifty.

(3) It is apt to attack the same individual again and again.

(4) It does not confine itself to one joint, but affects several simultaneously or in succession.

(5) It attacks also the membranes of the heart.

(6) It very rarely terminates in suppuration.

(7) It is not much benefited by measures calculated to relieve simple local inflammatory action, but is speedily subdued by proper constitutional treatment.

There is no possibility of explaining these peculiarities by any view which does not recognise the existence and operation of a generally acting internal cause.

(1) The hereditary transmission of the rheumatic tendency necessarily involves the idea of a constitutional, not a local malady. It means that a certain diathesis or particular state of the body predisposing to rheumatism is handed down from father to son. But such transmission can take place only in connection with constitutional ailments. We talk of a gouty, a rheumatic, a strumous, a cancerous diathesis, but never of a pleuritic, a peritonitic, or a nephritic one.

(2) The tendency to attack those of a particular age is a feature which is noted specially in connection with diseases owning a constitutional origin, and which is manifested in rheumatism, as it is in struma, gout, cancer, etc.

(3) The liability to repeated attacks in the same individual equally points to a constitutional predisposition.

(4) The fact that many joints suffer simultaneously or in succession points to a generally operating internal and constitutional cause. For it is most improbable that an external and local cause could habitually produce inflammation in so many different parts as suffer during a rheumatic attack.

(5) The tendency to heart affection can be explained only on the view that the true cause of the inflammation exists in the system. That cold and damp might give rise to an endo- or peri-carditis is possible; but that the occurrence of such inflammation in 33 per cent of the cases of acute rheumatism can be due to other than a generally acting constitutional cause is in the highest degree improbable.

(6) The rarity of suppuration, no matter how intense and prolonged the inflammation, indicates that rheumatic is essentially different from ordinary inflammation. "I have often known acute rheumatism of the severest kind have the start of the remedy, full ten days or a fortnight, during which nothing whatever has been done for its relief; and when at length the remedy has been applied, it has been cured as easily and rapidly as I could promise myself that it would have been had I taken it in hand ten days or a fortnight sooner.

"Surely here is something remarkable enough to make us stop and think for a moment. An inflammation of the brain, the liver, or the lungs would not thus wait our pleasure or our neglect, and be as curable ten days or a fortnight hence as it is to-day. For inflammation in these organs does not stand still. It is progressive from stage to stage, and each succeeding stage carries it farther and farther away from the remedy. But it is the very peculiarity of acute rheumatism that it *does*, in a certain sense, stand still.

All its actions and movements are simply as forcible and rapid as possible, yet does it stand still. All its energy is expended upon one stage, and there is no apparent progression beyond it. A fortnight ago there was great heat, and nervous and vascular excitement, and great pain and swelling of the joints; and, to-day, the heat and nervous and vascular excitement, and pain and swelling are exactly of the same amount as they were at first. There is no more sign of parts disorganised, or parts destroyed, now than then.”¹

(7) Finally, the success of constitutional, and the futility of local treatment, complete the proof that in rheumatism we have to deal with an ailment which owns an internal and constitutional, and not an external and local cause.

But though exposure to cold and wet are not *per se* the cause of acute rheumatism, there is ample evidence, the result of the accumulated experience of all countries and all observers, that such exposure often acts the part of an aider and abettor in determining a rheumatic attack. It does not itself give rise to the disease, but it renders the systems of those liable to be affected by the special cause of acute rheumatism more susceptible to its action. How it does so is one of the questions which we shall have to consider in connection with the different theories advanced as to the nature and mode of action of this special cause.

¹ *The Collected Works of Dr. P. M. Latham*, vol. i. p. 135. New Sydenham Society.

CHAPTER V

THE LACTIC ACID THEORY OF RHEUMATISM

BLOOD poisons may be divided into two classes : (a) those which are produced within the system ; and (b) those which enter it from without. The rheumatic poison is generally regarded as belonging to the former—as being some product of mal-assimilation, or imperfect tissue metamorphosis.

One of the characteristics of acute rheumatism is the occurrence of profuse acid perspirations. The urine, too, is hyperacid ; and even the naturally alkaline saliva may have an acid reaction. This excessive acidity naturally led to the hypothesis that an acid condition of the blood had something to do with the production of the rheumatic symptoms. Dr. Prout made the definite suggestion that the *materies morbi* was lactic acid, and that the rheumatic symptoms resulted from the accumulation of this acid in the blood. This idea, enlarged upon and developed by Todd, Fuller, and others, was regarded by the profession as affording of the causation of acute rheumatism a more satisfactory

explanation than any other hypothesis hitherto advanced. It possessed, moreover, the advantage of affording a definite foundation for a rational line of treatment—the treatment by alkalies.

The lactic acid theory was, for these reasons, very generally accepted, and for a long time was looked upon as quite satisfactory.

In time, however, the sufficiency of this theory began to be called in question, and doubts expressed as to the efficacy of the treatment by alkalies to which it naturally led. The failure of the alkaline treatment indeed, more than any other cause, tended to bring discredit on the acid theory.

Lactic acid is a product of tissue metamorphosis. It is an unstable compound which readily undergoes change, and is excreted by the lungs and skin as carbonic acid and water.

Its presence in excess in the system may be due to increased formation, to defective elimination, or to a combination of these two agencies. The most perfect development of the lactic acid theory is that which recognises this combination.

Lactic acid is formed during the metabolic changes which take place in muscle. During exercise it is formed in larger quantity than during quiescence; and when the exercise ceases, there is an excess of this acid in the system. But the exercise which causes increased formation of lactic acid, is accompanied also

by increased action of the lungs and of the skin, the channels by which the acid is eliminated, in the form of carbonic acid and water. Excessive formation is thus counterbalanced by increased elimination, and no accumulation takes place. But if, at this time, the action of the skin be checked, the metamorphosis and elimination of the lactic acid are arrested, it accumulates in the system, and the symptoms of acute rheumatism result. The action of the skin is checked by anything which chills the surface of the body.

Such is the most perfect development of the lactic acid theory; and such the manner in which this modern theory is combined with the old view as to the efficacy of a chill in the production of rheumatism. The theory is ingenious and beautiful, and by no means devoid of foundation. But it must not be accepted without a careful consideration of the evidence on which it rests.

The arguments adduced in support of this theory are the following:—

(1) Acute rheumatism is accompanied by excess of lactic acid in the system; the disease never occurs without such excess; and such excess is found only in connection with it.

(2) The injection of lactic acid into the systems of the lower animals has been said to be followed by inflammatory changes similar to those which occur in acute rheumatism.

(3) The administration of lactic acid to man has been followed by symptoms indistinguishable from those of acute rheumatism.

Let us consider each of these arguments.

1. *Acute rheumatism is accompanied by excess of lactic acid in the system, and such excess is noted only in connection with it.*

That no doubt is true; and the accuracy of the statement is not called in question. The point at issue is the relationship which this excess of acid bears to the rheumatic process. Is lactic acid the rheumatic poison, and does its presence in excess in the system give rise to the phenomena of acute rheumatism? Or is the excess of lactic acid, like pain and fever, merely one of that phenomena of the disease, one of the results of a morbid action set agoing by some other agency?

According to the lactic acid theory, this acid is the poison which causes the rheumatism. The main support of this theory is the fact which we are now considering, that there is always an excess of lactic acid in the system during the course of acute rheumatism.

But there are cogent reasons for not accepting the view that the acid is the cause of the rheumatism. For if it were so, the rheumatic symptoms should persist so long as the acid existed in adequate excess in the system, and should decline when it ceased to do so, and not till then. Remedies, too, which neutralise the acid should also cure the rheumatism; while

those which did not do so should fail to have any curative effect. The early advocates of the lactic acid theory believed that the administration of alkalies, by neutralising the acid, would cure the rheumatism. And theoretically such should have been the case. But the reality has been very different. For though, in the absence of any better mode of treatment, alkalies continued to be for many years the chief remedies administered in rheumatism, we very well know that they exercise little or no control over the disease. They may be given so as to saturate the system, and render the urine alkaline, without doing good to the rheumatism. The disease seems to last as long, and to run the same course when treated by alkalies, as it does when it receives no treatment at all. If the acid caused the rheumatism this should not be.

Again, we find that salicin and salicylic acid cure acute rheumatism effectually and speedily—as will be evidenced further on. It is impossible that their curative effect can be due to any neutralising action on lactic acid. Their effect is produced also independently of any action on the eliminating organs. It is certain that these remedies neither neutralise nor get rid of the acid; for in cases of acute rheumatism which are thus cured, the perspiration and the saliva often continue to give an acid reaction for four, six, or more days after fever, pain, swelling, and all symptoms of rheumatism, except this acidity, have

disappeared. This continued acidity of the perspiration, so long after the rheumatic symptoms have ceased, is no doubt due to the presence and excretion of acid formed during the continuance of the disease. It has an important bearing on its pathology. It indicates, first, that the acid in the system is neither neutralised nor destroyed by the remedy which neutralises the action of the rheumatic poison, arrests the rheumatic process, and puts an end to the disease.

Second, it shows that the mere presence of lactic acid in the system does not necessarily give rise to rheumatic symptoms.

Third, it indicates that it is the *production* of the acid in excess, not its mere *presence* in excess, which is essentially associated with these symptoms. In other words, these symptoms and the presence of lactic acid in the system would seem to be associated together as conjoint results of the rheumatic process. On this view of the matter, excess of lactic acid in the system becomes one of the ordinary symptoms of acute rheumatism—a result, and not the cause, of the morbid process which constitutes the disease.

2. *The injection of lactic acid into the systems of the lower animals has been said to be followed by inflammatory changes similar to those which occur in acute rheumatism.*

Many years ago Sir Benjamin Ward Richardson

published an account of some experiments made on cats and dogs by injecting lactic acid into their peritoneal cavities. The result of these experiments he regarded as favourable to the lactic acid theory of rheumatism ; and they have been referred to by various authors as one of the reasons for accepting that theory.

A careful perusal of Dr. Richardson's paper indicates that there has been accorded to his experiments a wider scope and greater significance than is their due. For in none of the animals experimented on was there induced a morbid condition which we would call rheumatism in man. What Dr. Richardson found, and all that he found, was, that in animals into whose systems lactic acid had been injected, there was observed, after death, what he regarded as evidence of inflammation of the endocardium. Endocarditis, and not rheumatism, was the malady induced. But as endocarditis is frequent, and an excess of lactic acid invariable, in acute rheumatism, the inference was drawn that these experiments demonstrated the accuracy of the view that lactic acid is the morbid agency which gives rise, not only to endocarditis, but also to the rheumatism with which endocarditis is usually associated. Granting for a moment the accuracy of Richardson's observations, the inference is wider than the facts warrant.

Moreover, a careful examination of these facts indicates very important points of difference between the condition noted by Richardson and that which

occurs in connection with acute rheumatism—so important that we are led to regard the results of his experiments as negative so far as the pathology of acute rheumatism is concerned, and the inferences drawn from them as inadmissible.

What Dr. Richardson teaches is, that in both induced and rheumatic endocarditis the cause of the inflammation is lactic acid in the blood; and that the acid produces its effect by a direct irritant action on the free surface of the endocardium.

The bearing of his experiments on our subject may be considered under the two following propositions taken from Richardson's paper:—

1. "Lactic acid could not exist in the blood without producing endocardial mischief."

2. "The action of the poison which produces the disease (rheumatic endocarditis) is directly on the free surface of the endocardial membrane; the poison acts, in a word, after the manner of a local irritant."

(a) The first proposition, that lactic acid could not exist in the blood without producing endocarditis, is at variance with facts and experience.

"It is absurd," says Richardson, "to assume that ounces of an acid of the producing series thrown off from the skin of a sick man should not be derived from his blood." Lactic acid is thus thrown off from the skin in acute rheumatism. If Dr. Richardson's proposition were correct, endocarditis should be an

invariable complication of that disease. But it occurs only in a minority of cases—about 30 per cent. Lactic acid, therefore, exists in excess in the blood, without producing endocardial mischief in about 70 per cent of the cases of acute rheumatism which occur.

(*b*) The second proposition, that lactic acid acts as a local irritant to the endocardium, is in keeping with the first; but is equally inconsistent with evidence. If lactic acid be the rheumatic poison, and if it exercise a direct irritant action on the endocardium, that membrane should give evidence of inflammation in every case of acute rheumatism; but such inflammation occurs in only a minority of the cases. Again, if this were its mode of production, the inflammation should be diffused over the whole surface of the endocardium; but it is limited to the valvular portion of that membrane, and even there is found only on one side—in the aortic valve only on its convex surface, and in the mitral only on its auricular.

The pathogenesis of rheumatic endocarditis ought not to, and cannot rightly, be considered apart from that of the joint inflammation in connection with which it occurs. The poison which gives rise to the one, gives rise to the other; and its mode of action in the production of inflammation of the fibrous and serous tissues of the joints and of the heart is doubtless the same. It is physically impossible for lactic acid to act on the fibrous elements of the

joints as Dr. Richardson believes that it acts on the endocardium.

Again, pericarditis is almost as frequent in acute rheumatism as endocarditis. The two are due to the same cause, and produced in the same way ; but Dr. Richardson leaves pericarditis out of account altogether, and gives of the occurrence of inflammation of the membrane which lines the interior of the heart, an explanation which cannot apply to inflammation of that which invests it externally.

For these various reasons, we regard the inferences which have been drawn from Dr. Richardson's experiments as fallacious and unwarranted ; and the experiments themselves as affording no valid support to the lactic acid theory of rheumatism.

The results of experiments made on the lower animals may readily have their importance exaggerated ; and we cannot exercise too great caution in drawing from them inferences applicable to man. Though certain effects are got from the administration of this or that drug to a cat or dog, it by no means follows that like results would follow its administration to man. This objection is peculiarly applicable to Dr. Richardson's experiments. There are abundant observations to show that the only invariable result of the administration of lactic acid to man is increased action of the skin. But this is a result which could not be got in dogs, for they do not perspire.

But above and beyond these very cogent reasons for rejecting Dr. Richardson's teaching there is another one even more potent. It has been demonstrated by Reyher¹ that the endocardial signs which Dr. Richardson attributed to the action of lactic acid are found in all dogs, no matter how they are killed. Richardson and Rauch, who supported him, omitted to take the elementary precaution of satisfying themselves before making their experiments as to what was the normal condition of the endocardium in the dog. Had they done this, they would have found it to be exactly that which they described as morbid, and as the result of the action of lactic acid on it. Redness of the endocardial lining of the right side of the dog's heart which Richardson regarded as pathological, and as the result of the direct irritant action of lactic acid, is the normal condition of that membrane, no matter how death is brought about.

Richardson's observations and the inferences drawn from them may, therefore, be set on one side.

3. *The administration of lactic acid to man has been followed by symptoms of acute rheumatism.*

Since Cantani recommended lactic acid as a remedy in diabetes, numerous cases of that disease have been thus treated. In several the administration of the acid has been followed by symptoms indistinguishable

¹ Virchow's *Archiv.*, Band xx. ; and *British and Foreign Medico-Chirurgical Review*, January 1862.

from those of rheumatism, pain and swelling of joints, with rise of temperature.

One of the most remarkable is a case related by Dr. B. Foster,¹ in which there occurred six well-marked arthritic attacks. "The phenomena corresponded in all respects to those which are characteristic of acute articular rheumatism. They came on when the acid was taken, and ceased when it was discontinued. When moderate quantities of the acid were tolerated, an increase in the dose was succeeded by the painful inflammation of the joints. Coinciding with the development of the articular affection was the appearance of perspiration, at first only slight, but afterwards, in the more severe attacks, copious and acid. "These facts," continues Dr. Foster, "have dispelled the last lingering doubt in my mind as to the truth of the lactic acid theory of rheumatism."

One cannot read the details of Dr. Foster's cases without feeling that we have in their facts strong evidence in support of the lactic acid theory—to my mind, the strongest that has been adduced in its favour. Such evidence cannot be disregarded or ignored; either we must explain it, or our refutation of the lactic acid theory must remain imperfect and inadequate. Can it be explained? I think it can; and that even Dr. Foster may be shaken in his renewed allegiance to his old love.

¹ *Clinical Medicine*, by Dr. B. Foster, 1874.

Lactic acid is a product of tissue metabolism—an excretory product, therefore. Such products, when retained unduly in the system, exercise two distinct actions—first a stimulant action on the organ by which they are normally eliminated; and second, a disturbing action on the tissues which supply the materials from which they are formed. The retention, for instance, of an excess of carbonic acid in the system causes, first, increased force and frequency of respiration, and ultimately paralysis of that function and asphyxia. Excess of urea in the blood causes, first, increased action of the kidneys, and ultimately that condition of tissue asphyxiation to which we apply the term uræmia. So with lactic acid, its retention in the system causes, first, increased action of the organ by which it and its products are normally eliminated, the skin; and second, functional disturbance of the textures during whose retrograde metamorphosis it is formed, if for any reason the eliminating organ fails in its duty. Lactic acid is formed during the action and retrograde metamorphosis of the tissues of the motor apparatus, and is eliminated by the skin. The effects which we should expect to result from an excess of lactic acid in the blood are, therefore, increased action of the skin; and, failing that, functional disturbance of the motor apparatus. And that is exactly what Dr. Foster observed.

Lactic acid is so readily oxidised and eliminated, that it is only in exceptional cases that ingestion can

exceed elimination. Hence it is only in exceptional cases that its internal administration can give rise to disturbance. One of these exceptional cases is that recorded by Dr. Foster. The patient was suffering from diabetes and phthisis—both of them ailments accompanied by imperfect oxidation. “In diabetes,” says Dr. Foster, “we have a state of disordered nutrition very unfavourable to the conversion by oxidation of new compounds; and in Wright’s case this was aggravated by the serious pulmonary complications. Associated with this was a dry branny state of the skin highly unfavourable to the elimination of the lactic acid by one of the common channels.”

Lactic acid given under such circumstances—given, that is, to a man in whose system it cannot be oxidised, and by whose skin it cannot be eliminated—must be retained, and cause disturbance of the nutrition of the textures of whose metamorphosis it is a product. An excess of lactic acid in the blood checks the retrograde metamorphosis of these textures, and so disturbs their whole nutrition, just as retained excreta produce a corresponding action on the brain, and as an atmosphere of carbonic acid interferes with the elimination of that gas from the system. The symptoms resulting from the retention of lactic acid in the blood are, therefore, likely to be those of functional disturbance of the tissues of the motor apparatus.

Functional disturbance declares itself in different ways in different organs. In the brain it causes

nervousness, irritability, headache, giddiness, delirium, convulsions, and coma. In the heart it gives rise to more or less disturbance of the rhythm and force of its action. In the digestive organs it declares itself by evidences of imperfect and deranged digestion. In fibrous tissue the evidence of its existence is pain, which may be very severe, and is well exemplified by what is felt when a ligament is unduly stretched, or when, as in acute rheumatism, it is the seat of inflammation.

A disturbing agency like lactic acid, which acts on both the muscular and fibrous textures, will declare itself chiefly by symptoms referable to the latter. It will do so, because these textures give more ready and decided evidence of functional disturbance; and because any weakening of the muscles to which it might give rise, would be lost in the muscular debility and wasting, characteristic of the diabetes for which the acid was given.

Pain localised in the muscular and fibrous tissue of the motor apparatus is, therefore, the chief symptom which we should expect to find follow the retention in the blood of an excess of lactic acid. And so in reality it is found to be.

The general result of Dr. Foster's evidence is to show that lactic acid causes increased action of the skin; and, failing this, disturbed nutrition and consequent irritation of the muscles and the fibrous textures of the joints.

But, it may be said, if you grant this—if you admit that excess of lactic acid in the blood may give rise to articular pains—do you not thereby admit the truth of the lactic acid theory of rheumatism? By no means; the two propositions are not only not identical, but are widely different. That excess of lactic acid in the blood is the cause of some of the phenomena of acute rheumatism, is a position which I not only admit, but am prepared to maintain. But that is a very different thing from saying that it causes all its phenomena, which is what the lactic acid theory asserts. That theory is, that lactic acid is *the rheumatic poison*, the special *materies morbi* which initiates and sets agoing all the phenomena of the disease. One of these phenomena is the presence in the blood of an excess of lactic acid. But lactic acid cannot be the cause of its own increased formation—of its own excess. The position is an absurd one; but its very absurdity serves to demonstrate the weakness of the lactic acid theory, and to bring before us the real nature of the question which we have to consider, and of the difficulties which we have to face.

The advocates of the lactic acid theory of rheumatism have taken one of the phenomena of the disease, and have raised it from its normal and subordinate position of a symptom to the rank and dignity of an exciting cause. In so doing they have necessarily fallen into error. Excess of acid may cause joint

pains, but what causes the excess of acid? That has to be explained, no less than the phenomena which combine with it to form the symptoms of acute rheumatism.

And herein we see the inadequacy of Dr. Foster's observations to throw light on the ultimate pathology of the disease; and the shortsightedness of the view which regards them as doing so. In his cases the lactic acid was given to the patient, and its presence in excess was readily accounted for. In acute rheumatism the excess of lactic acid is the phenomenon which, of all others, it is at once most essential and most difficult to explain. If the first requisite to the production of rheumatism be an excess of lactic acid, the first requisite to a satisfactory theory of rheumatism is that it should account for this excess. An attempt to do so has been made by some of the advocates of the lactic acid theory, notably by Corrigan and Senator. Lactic acid, they say, is formed during muscular exercise. Under ordinary circumstances it is partly oxidised and got rid of as carbonic acid and water; partly, when there is a great deal of it, excreted unaltered in the sweat. Should the cutaneous surface be chilled, the elimination of the acid will be checked, and it will accumulate in the system.

That chilling of the surface when heated by exercise may be followed by a rheumatic attack there is no doubt. But to be heated by exercise is so common

at the age at which acute rheumatism chiefly occurs, and to be exposed to cold so common in the climate in which it most prevails, that great allowance has to be made for the elements of chance and accidental coincidence. But making allowance for these, there can be no doubt that overheating and subsequent exposure to cold, and even such exposure without previous overheating, do in some cases seem to determine a rheumatic attack. But it does not follow that the determining agent is the checking of the action of the skin. Overheating and subsequent chilling are not the only effects of exercise and subsequent exposure; they are not even the most common. A more constant and more important one is exhaustion; and the probable explanation of the connection which obtains between the exercise and the rheumatism is that the exhaustion consequent on the exercise renders the system more susceptible to the action of the rheumatic poison. The depressing influence of cold by lowering the whole vitality would lead to the same result.

A greater liability to the action of certain morbid agencies, when the system is exhausted, or depressed from any cause, has been noted in connection with many diseases. Referring to malarial fevers, with which, as we shall by and by see, rheumatic fever has many analogies, Niemeyer says: "Exhausting exercises and other debilitating influences, errors of diet, and particularly catching cold, increase the predisposition

so much, that persons who have long been exposed to malaria with impunity, are not affected by it till one of these causes has acted on them."

In the case of acute rheumatism, it is not so much the exercise as the exhaustion which follows it; it is not so much the chilling of the surface as the depressing action of the cold on the system, which are the disturbing agencies. They do not themselves produce the disease, but they render the system more liable to the action of the rheumatic poison.

There are other cogent reasons for rejecting the view, that chilling of the surface plays the part attributed to it in the production of acute rheumatism. In the first place, it is to be noted that chilling of the surface when heated by exercise is frequently had recourse to with impunity, if not with actual benefit. Then again, if we regard sudden chilling of the surface as a danger, and as a cause of acute rheumatism, how are we to explain the beneficial action of the cold bath in the hyperpyrexia of malignant cases of that disease? Here we have the malady presenting itself in the most distinct form: lactic acid is being freely thrown off by the skin, the patient is in imminent danger, and yet the only thing which does him good—the only thing which seems to give him a chance of recovering—is to apply cold to the surface, thereby not only lowering the temperature, but checking also the action of the skin. The same agency which is blamed for causing the patient's illness, is applied in a more

decided manner to get him out of it, and is really the only reliable means of attaining this end.

This theory as to the mode of production of acute rheumatism, and of the operation of cold, has other inherent weaknesses. If it means anything at all, it means, first, that during half an hour's violent exercise there is formed in the systems of those of rheumatic constitution enough lactic acid to produce an attack of acute rheumatism; second, that every time they take active exercise such persons are liable to be laid up by that disease; and third, that they are saved from such a misfortune only by the free action of their skins.

But still more is involved in this belief; for if we adopt it we must also believe that during half an hour's violent exercise there is produced in the system enough lactic acid, not only to give rise to acute rheumatism, but to keep up the symptoms of that disease for weeks, and to supply at the same time the excess of acid which is being eliminated during the whole period of the continuance of the malady. The mere statement of what is involved in this belief suffices to condemn it. For to suppose that the whole of the lactic acid which is required to produce an attack of acute rheumatism of several weeks' duration, with its accompanying profuse acid perspirations, could be produced in the system in the course of half an hour, is to presuppose the existence in the system at the end of that half-hour of a quantity of lactic acid which (granting that acid to be the cause of the rheumatism)

would produce the most acute inflammation of all the tissues of the body liable to rheumatic inflammation, and kill the patient by such inflammation in two or three days. On this view of its causation and nature all cases would be acute, and the disease more formidable and fatal than it is.

Again, if the poison of the disease were thus produced—if the whole of the *materies morbi* existed in the system at the commencement of the attack—which would be the case if the above view were correct—we should find the symptoms of acute rheumatism developed, not gradually as is the case, but quickly, and very soon after the chill was applied; we should have the joints affected, not in succession as is the case, but all at the same time, and also very soon after the chill; and we should have the heart involved in every case. We should find, too, that the free action of the skin, and consequent elimination of the acid, which characterises the disease, would be followed by relief of the pain; and that we know is not the case.

No, it is simply impossible that the gradual onset of the symptoms of acute rheumatism, the protracted and varying course of the disease, the shifting character of the joint inflammation, and the long-continued hyperacidity of the secretions, can result from such an excess of lactic acid as could be produced in one, or in a dozen hours' violent exercise. In an attack of acute rheumatism there is eliminated by the skin alone

in twenty-four hours a quantity of acid greater than is likely to exist in the system at the end of an hour's exercise.

It is erroneous and misleading to regard the excess of lactic acid, which undoubtedly does exist in acute rheumatism, as simply an accumulation. The use of this term, and the undue importance attached to the operation of cold, have led to a misinterpretation of the phenomena observed. What we mean when we say that an excretory product accumulates in the system, is that it is being formed but not properly eliminated. But in acute rheumatism there is increased elimination of lactic acid; and this increased elimination goes on during the whole course of the malady. The most severe cases, those in which there is most suffering, and most of the characteristic joint affection, are also those in which the perspiration is most profuse and most markedly acid; and in which, therefore, the acid is most freely eliminated. We cannot say that in such circumstances there is any accumulation of lactic acid in the system; for it is being eliminated in unusual quantity. Such increased elimination points, not to accumulation, but to increased formation; and *this* is the phenomenon which calls for attention and for explanation. Increased formation of lactic acid is one of the essential features of acute rheumatism; and no theory of that disease can be regarded as satisfactory, which does not recognise and account for this increase. This the lactic acid theory fails to do.

Other symptoms of the disease, too, this theory not only does not explain, but does not even take cognisance of.

In advancing a theory of the causation of acute rheumatism, we have to account, not only for the occurrence of the joint pains, the febrile disturbance, and the acid sweats, but for the occurrence of the symptoms which precede these special and characteristic manifestations of the fully developed disease; and precede even the evidence of the existence of an excess of lactic acid. A case of acute rheumatism does not leap at once *in medias res*. The characteristic symptoms of the disease are preceded often for two, three, or more days by shivering, *malaise*, a sense of weakness accompanied by aching of the limbs. These initial symptoms are as much a part of the ailment as the joint pains which they usher in, and have equally to be accounted for. This the lactic acid theory does not even attempt to do.

But while we reject the view which regards lactic acid as the cause of rheumatic fever, as the morbid agency which originates the disease, we are far from regarding that acid as without action, and as having no share in the production of the phenomena of a rheumatic attack. An excess in the blood of any product of retrograde tissue metamorphosis could scarcely be without some action. And there can be no reasonable doubt that the profuse perspirations which form a characteristic feature of the disease, are

mainly due to the stimulant action on the skin of the excess of lactic acid in the blood. It is probable, too, that should formation exceed elimination, the resulting excess of acid would tend to exaggerate the already existing disturbance of the fibrous tissues, and so aggravate the pains and general symptoms of the malady.

We shall by and by see that there is reason to suppose that cases in which the fibrous tissues have been weakened and rendered irritable by frequently repeated rheumatic attacks, may have their convalescence retarded, and the ailment prolonged, by the action of the acid on the altered fibrous tissues.

CHAPTER VI

THE NEUROTIC THEORY OF RHEUMATISM

ONE of the most prominent and popular of modern physiological doctrines is that which teaches that every physiological act and every normal function is carried on under the controlling influence of the nervous centres.

A doctrine at once so simple and so far-reaching could not fail to attract the physician, and to be applied by him to the explanation of some of the phenomena with which he has to deal. If such and such a function is dominated by a special nervous centre, and is dependent for its due performance on the integrity of that centre, may not the derangements of that function which are noted in disease be the result of disturbances originating in its dominating centre? The general doctrine thus formulated evidently admits of wide application. Theoretically, there is scarcely any disorder of function to which it might not be applied with some degree of plausibility; and there is considerable danger of our being seduced into the too free utilisation of so simple

a doctrine in explanation of morbid phenomena. Against this danger we must be on our guard.

An instance of the ready appropriation of this doctrine by pathologists we have in one of the modern views of the causation of fever. Physiology teaches that the nervous centres exercise a controlling influence over the heat of the body; and clinical research has demonstrated that some injuries and non-inflammatory lesions of the nervous centres cause a rise in the temperature of the body. The increased body heat noted in such cases is clearly of neurotic origin; and the demonstration of the occurrence of such rises of temperature naturally suggests a neurotic theory of fever. But the attempt to explain by this theory the occurrence of all forms of pyrexia is an instance of the too free application of the doctrine in question. Because in some cases increased body heat is of neurotic origin, it does not follow that all fever is so. The inference is wider than the facts warrant. Still it has been drawn, and this view advocated, erroneously I think, as I have elsewhere¹ endeavoured to show, by competent men.

Another example of the free application of this doctrine to the explanation of the phenomena of disease—that which specially concerns us at present—we have in the attempt to explain by it the occurrence of rheumatic inflammation of the joints.

It is an established fact in pathology that joint

¹ *Fever: A Clinical Study*, by T. J. MacLagan, M.D. (Churchill), 1888.

troubles do occur as a sequence of lesions of nerves and nerve centres. Charcot,¹ describing them as they occur in connection with brain lesions, says that they are chiefly found in cases of hemiplegia, where the paralysis is consequent on encephalitis or brain-softening. Brown-Sequard,² referring to the pain sometimes experienced when paralysed limbs are pressed upon or moved, says that such pains "depend upon a subacute inflammation of the muscles or joints, which is often mistaken for a rheumatic affection."

Dr. J. R. Mitchell,³ as far back as 1831, called attention to joint changes occurring as a sequence of injuries of the spine. More recently, attention has been prominently directed to this subject by his son, Dr. Weir Mitchell,⁴ who describes the "curious inflammatory states of the joints" which follow injuries to nerves, especially those of the arm.

Then again, as research has advanced and knowledge increased, it has become more and more certain that rheumatoid arthritis is a disease *per se*, quite distinct from both gout and rheumatism, both in its clinical history and in its pathology; and the special attention which as a separate ailment it has received has led pathologists more and more to lean to the view originally advanced by Remak, that the joint

¹ *Lectures on Diseases of the Nervous System.*

² *Lancet*, vol. ii., 1861.

³ *American Journal of Medical Sciences*, vol. viii.

⁴ *On Injuries of Nerves.*

changes which form its characteristic feature are somehow or other the result of malnutrition consequent on weakening of nerve centres.

With the growing belief in the doctrine of the localisation of cerebral function, and of the part played by nerve centres in controlling and regulating the functions of organic life; with such distinct evidence as we have that joint changes do take place as a consequence of lesions of nerves and nerve centres, and with the mind of the profession all but made up that rheumatoid arthritis is of neurotic origin, it was inevitable that we should ere long hear of a neurotic theory of rheumatism. Such a theory was indeed suggested by the elder Dr. Mitchell, but the suggestion lay dormant till increasing knowledge of the subject to which he drew attention, the occurrence of joint troubles as a sequence of nerve lesions, combined with the results of the separate study of the pathology of rheumatoid arthritis, led to its revival.

By most of those who advocate this theory, the disturbance of the nerve centres is believed to be produced by peripheral irritation applied to surface nerves, and transmitted by them to the nutrition centres of the joints. That joint troubles might thus be induced there can be no doubt; but that acute rheumatism could be so caused seems to me highly improbable. For in the first place, acute inflammation, such as that which characterises the

joint affection of that disease, is not the form of joint trouble which we find associated with lesions of nerves and nerve centres. Nor can it be regarded as *à priori* other than highly improbable that such acute sthenic inflammation should be the result of malnutrition. And, in the second place, inflammation of the joints is not the only thing with which we have to deal in acute rheumatism. The disease has other features and other phenomena calling for explanation as much as do the joint lesions. If, for instance, as is maintained, cold be the common cause of the peripheral nerve irritation which sets the malady agoing, why is the disease more common in temperate than in cold climates? Why is it most common at the age at which the power of resisting cold is greatest—fifteen to fifty? And why so rare among children and old people, whose power of resisting cold is so much less? Again, how on this view are we to explain the invasion of fresh joints, after the patient has been warm in bed for days, maybe for weeks? How account for the occurrence of endocarditis and pericarditis? Why is the endocarditis so limited in extent? Why does it affect only the valves of the left side, and only one surface of the valve? How account for the excess of lactic acid in the system? These are all points of which an explanation must be given; and no theory of rheumatism can be regarded as satisfactory which does not do so. But the neurotic theory

takes no cognisance of the heart trouble, and offers of the joint inflammation an explanation which fails to deal with some of the characteristic features of that lesion.

The fact is that the phenomena of acute rheumatism are such as can be explained on no view which does not recognise the action of a poison which is produced in the system during the course of the malady, and circulates in the blood. Recognising this, Dr. Latham, one of the most strenuous and able advocates of the neurotic theory, advanced the view that, as a result of exposure to cold, there is produced a hyperæmic state of the muscles; that from this there results an increased formation of glycocine; that this is ultimately transformed in the liver into uric acid; and that this uric acid it is which, by impairing the action of the nutrition centres of the joints, causes the inflammation noted in acute rheumatism. According to this view, uric acid with some aid from lactic acid causes rheumatism much as it causes gout.

The objections to this very ingenious theory are all those which have been already advanced against the original form of the neurotic theory; and in addition, the fact which has been demonstrated by Garrod and others over and over again, that uric acid does not exist in excess in the blood in acute rheumatism. It is an acid which, when it does exist there in excess, is very easily detected.

Before we can accept the view that the symptoms

of acute rheumatism are in any way associated with an excess of uric acid in the blood, it must first be demonstrated that such excess exists. But the demonstration is quite the other way. Garrod's observations on this point are fatal to Dr. Latham's hypothesis. He has distinctly shown that the blood in acute rheumatism does not contain an excess of uric acid; as the assumption of such excess is an essential part of Dr. Latham's theory, and as such excess does not exist, this theory falls to the ground.

It may be laid down as a general rule in science that when we have to advance several hypotheses to explain one set of phenomena we are almost certainly on the wrong track. Dr. Latham's theory bristles with hypotheses. The ability with which he manipulates them does not remove the weakness and inherent improbability imparted to his theory by their number.

Of all acute febrile ailments acute rheumatism is the one in which the nervous centres give least evidence of disturbance. In typhus and typhoid fevers, scarlet fever, pneumonia, etc., there are generally symptoms distinctly and directly referable to disturbance of the brain. In rheumatic fever such symptoms seldom occur except in cases of hyperpyrexia, and in cases complicated with acute carditis or pericarditis, and in these the nervous symptoms are due to special causes, and have no connection with the joint troubles.

Neither the clinical features nor the natural history of acute rheumatism supports the view that

the disease is of neurotic origin. As Arnozan remarks, "avant de prononcer que les lésions articulaires du rhumatisme sont des lésions trophiques dépendant de la moelle, il faudrait démontrer d'abord que celle-ci est réellement atteinte."¹

Pathological analogies have been inferred between gout, rheumatism, rheumatoid arthritis, and spurious arthritis, because the joints are affected in each. We must be careful to distinguish between clinical and pathological analogy, or we shall fall into pathological error.

The joint troubles referred to represent four different ailments as distinct in their pathological histories as are pneumonia, bronchitis, asthma, and pulmonary emphysema. Because these ailments consist each in some form of pulmonary trouble we do not infer pathological analogies between them, or refer each to disorders of the respiratory centre. Though we look upon asthma as a disease of the nervous system, we do not say that bronchitis is so to. During an attack of either ailment the calibre of the bronchial tubes is diminished, and their functional utility interfered with, but we do not allow such clinical analogies to blind us to the fact that the two ailments have no pathological affinity.

The joint troubles which result from nerve lesions bear to acute rheumatism no closer resemblance, either

¹ Arnozan, *Des lésions trophiques consécutives aux maladies du système nerveux*, p. 110. Paris, 1880.

clinically or pathologically, than asthma does to acute bronchitis; and a careful consideration of all the evidence leads to the conclusion arrived at by Arnozan that "les rapports entre le système nerveux et le rhumatisme articulaire sont encore à trouver." (*Op. cit.*, p. 111.)

CHAPTER VII

THE MIASMATIC THEORY OF RHEUMATISM

IN rejecting the neurotic theory of rheumatism, we reject the view that the disease is due to disturbance originating independently of a special poison.

In rejecting the lactic acid theory, we reject the view that the rheumatic poison is generated within the system.

The only alternative view is that this poison enters the system from without.

Of such poisons there are two kinds—the contagia and the miasmata. What knowledge we possess regarding the nature and mode of action of these poisons has been got less from a study of the poisons themselves than from a study of the phenomena to which they give rise. The essential properties of the fevers to which the contagia give rise are as follow :—

(1) They are communicable from the sick to the healthy.

(2) They have a fixed and definite period of duration.

(3) One attack, as a rule, confers immunity from a second.

But rheumatic fever is not communicable from the sick to the healthy ; it has no fixed period of duration ; and one attack confers no immunity against a second.

As rheumatic fever bears no analogy to the contagious fevers, its poison cannot be regarded as a contagium.

There remain the miasmata. In studying malarial fevers, the facts which force themselves most prominently on our attention are as follow :—

(1) They are most apt to occur in low-lying, damp localities, in certain climates, and at certain seasons of the year.

(2) Some people are more liable to be attacked than others.

(3) They have no definite period of duration.

(4) They are not communicable from the sick to the healthy.

Now we cannot fail to see that these are quite the attributes of rheumatic fever. It is most common in temperate climates, at certain seasons, and in damp low-lying localities. It has no fixed period of duration. It is not communicable from the sick to the healthy. Some people are more liable to suffer than others ; and its poison, we have seen reason to believe, enters the system from without.

But the analogy between rheumatic fever and the common malarial fevers does not end here. A still further analogy may be traced in their clinical histories.

(1) Malarial fever is irregular in type, and char-

acterised by variations in its course. So is rheumatic fever.

(2) Profuse perspirations characterise the course of malarial fevers; so they do that of rheumatic fever.

(3) During the course of malarial fevers the urine is loaded with urates; so it is in rheumatic fever.

(4) One attack of malarial fever seems to render the system more liable to its recurrence. The same is true of rheumatic fever.

(5) Malarial fevers often leave an impress on the system, which renders the sufferer liable to disturbance and the recurrence of some of their symptoms from slight causes. Rheumatic fever often has the same effect.

(6) Unless arrested by treatment, malarial fevers are apt to have a protracted and uncertain course. So is rheumatic fever.

(7) The course of malarial fever is speedily arrested by large doses of cinchona bark. The course of rheumatic fever is as speedily checked by large doses of willow bark.

It is evident that the rheumatic poison, both in its history, and in its effects on the system, bears a closer analogy to the poison of malarial fevers than to any other morbid agency.

The poison which gives rise to malarial fever, and that which gives rise to rheumatic fever, are distinct and separate agencies. But the analogies noted in the natural history and course of the ailments which they

respectively produce, are sufficiently close to indicate the probability of their being allied in nature and in mode of action.

The symptoms, course, and pathological lesions of rheumatic fever do not differ from those of intermittent and remittent fever, more than do the symptoms, course, and pathological lesions of typhoid fever from those of typhus and of relapsing fever. We do not allow the difference in the maladies produced to blind us to the fact that the poisons of typhus, of relapsing fever, and of typhoid fever are allied in nature and in mode of action. The differences noted between malarial fever and rheumatic fever at the bed-side and in the *post-mortem* room, need be no hindrance to our regarding their poisons as possessed of like analogies.

The existence of some points of analogy between intermittent and rheumatic fever did not escape the notice of some of the older observers. Haygarth "thought that there were several analogies between an ague and a rheumatic fever. In both diseases the urine lets fall a similar lateritious sediment. In intermittent as well as rheumatic fever the blood when let is covered with an inflammatory crust. The pain and fever of rheumatism have certain periodical, though not quite regular, paroxysms and intermissions."

Acute rheumatism is generally regarded as a continued fever. But, except its prolonged duration, it possesses none of the characteristics of such a fever.

The continued fevers have a regular and continuous course, a typical and characteristic range of temperature, and a definite period of duration. Often they terminate by a distinct crisis. Rheumatic fever has none of these characteristics. Its course is irregular. It has no definite period of duration ; and no typical range of temperature. It never terminates by a distinct crisis ; and it is impossible to say how long a case may last if left to pursue its natural course. Seeing a man suffering from one of the continued fevers, one can foretell with tolerable certainty the future course and duration of the malady. In rheumatic fever this cannot be done. He may get well in one week or the fever may last five or six. To-day the temperature may be 104° , and the joints acutely inflamed ; a couple of days later the temperature may be 100° , and the joints much better. A few days afterwards the acute symptoms may have again returned, and the fever be as high as ever. And so it may rise and fall, and rise and fall, every few days for several weeks in succession ; or the disease may come to a termination at the end of eight or ten days. Irregularity is the prominent feature of both the course and the duration of acute rheumatism. "Irregular pyrexia is joined with irregular perspirations" (Scudamore).

It is evident that this fluctuating course is more like that of remittent and intermittent than that of the continued fevers.

There are reasonable grounds, it will be seen, for

regarding rheumatism as malarial in nature ; and its poison as a miasm which enters the system from without. The further prosecution of our inquiry necessitates a preliminary investigation into the nature of malarial poisons generally.

CHAPTER VIII

ON THE NATURE OF MALARIA

“I HAVE no hesitation,” says Niemeyer, “in saying decidedly that marsh miasm—malaria—must consist of low vegetable organisms.” Though when Niemeyer wrote these words, our knowledge of the nature of malaria scarcely warranted so decided a statement; the evidence which has accumulated since then all tends to show that Niemeyer was right.

Lanzi and Terrigi,¹ Klebs and Tommasi-Crudeli,² made a number of observations and researches in the malarial district of the Agro Romano, near Rome, which led them to believe that the malarial poison is an organism which may be obtained from the soil, and may be cultivated in the bodies of animals.

Laveran, whose researches were carried on in Algiers, found that the blood of those suffering from malarial fever contained (1) crescentic pigmented bodies, (2) pigmented bodies in the red corpuscles, and (3) pigmented flagellate organisms. These different forms he regarded as different phases in

¹ *Centralblatt f. Med. Wiss.*, 1875.

² *Allg. Wien. Zeit.*, 1879.

the development of an organism which he believed to be the malarial poison—the cause of the disease. These observations have been confirmed by other observers. Osler describes (1) amœboid bodies in the red corpuscles; (2) pigmented bodies in the red corpuscles; (3) larger solid bodies in the interior of vacuoles; (4) free pigmented crescents, which may sometimes be seen to develop in the interior of the red corpuscles; (5) rosette forms; (6) scattered small bodies resulting from segmentation of the rosettes; (7) flagellate organisms, round, ovoid, or pear-shaped, with finely granular protoplasm; (8) small round pigmented bodies one-fourth to one-half the size of the red corpuscles.

The amœboid and pigmented bodies, though met with in both acute and chronic cases, seemed to be chiefly associated with acute manifestations of the disease; while the crescents were noted chiefly in chronic cases and in the later stages of acute cases. Quinine always caused the pigmented bodies to disappear.

Councilman's observations run on all fours with those of Osler. The segmented organisms he found chiefly just before and during the cold stage. The crescentic form he found only in malarial cachexia. All forms he found most abundantly in blood taken from the spleen. The effects of quinine on these organisms were carefully noted by him. The administration of this drug in large dose always

caused the segmented organisms to disappear; while on the crescentic it had no particular effect.

The researches of Golgi, Manson, and others have further verified the accuracy of Laveran's observations, and strongly support the view advocated by him, and now generally accepted by the profession, that the organisms which he found in the blood of those suffering from malarial fever are really the poison which gives rise to the disease.

If such be the case, the phenomena of malarial fever must be such as an organism would produce; and a detailed consideration of these phenomena should lend support to Laveran's view. How does the plasmodium malariae cause the phenomena of malarial fever?

CHAPTER IX

THE MODE OF ACTION OF MALARIA

THE malarial poison is an organism which is largely reproduced in the blood during the course of the fever to which it gives rise. To this reproduction of the poison in the system the fever is due. The phenomena of these fevers are, indeed, such as can be explained only on this view of their nature and mode of action. A short residence, even one night, in a malarial district may give rise to a fever of some weeks' duration. If during one night the sufferer inhaled enough poison to cause an attack of fever so prolonged—if the whole of the poison requisite to the production of such an illness existed in and acted on the system at the commencement of the attack, the sufferer should be speedily killed by a dose of poison competent to produce such an illness. Moreover, if the poison were all taken into the system at once, if the whole of it existed there at the commencement of the attack, not only would the full effects of the poison be produced at once, but malarial fevers would lose their intermittent and remittent character, and their

phenomena be concentrated into a violent and continued fever, recovery from which would be the exception. It does not seem possible to explain the phenomena of these fevers on the supposition that the whole of the poison necessary to their production exists in the system at the time of onset of the malady. Their varying and intermittent course, their prolonged duration, and their small mortality can be accounted for only on the view that their poisons are reproduced during their course, and that this reproduction takes place in an intermitting manner. The researches of Laveran and others just referred to have, indeed, demonstrated that such is the case; for the poison (the *plasmodium malarizæ*) is found abundantly in the blood during the pyrexia, but not during the apyrexia. How does this organism give rise to such a result; how can the reproduction of an organism in the blood cause the phenomena of the malarial fevers?

All organisms exercise a definite action on their environment. The environment of these organisms is the blood and the tissues of the body. What we have now to do is to consider what the action of these organisms on their environment is, and whether or not such action would suffice to cause the phenomena of malarial fever. The special phenomena which have to be considered are—

- (1) The occurrence of fever; and
- (2) The occurrence of remissions and intermissions in this fever.

All organisms consume nitrogen and water. These they derive from their environment. The plasmodium malariae, therefore, consumes the nitrogen and water of the blood and tissues. But as nitrogen and water are the chief elements required for the nutrition and repair of the tissues, such an action must have serious effects on the system.

That the reproduction in the system of minute organisms having such an action is competent to cause the essential phenomena of fever I have elsewhere,¹ in the case of the continued fevers, shown in some detail.

Increased consumption of water causes thirst, dry skin, and scanty urine. Increased consumption of nitrogen means increased metabolism, rise of temperature, increased rapidity of circulation, quick pulse, increased formation and elimination of urea, wasting of the nitrogenous tissues; and these are all the essential phenomena of fever. The nitrogen and water which ought to go to nourish the tissues are in great part taken up by these minute organisms. Give as much nitrogenous food, as much milk and beef-tea as you please, the tissues still waste. Give as much water as you please, the thirst, the dry skin, and the scanty elimination of water continue. Water is taken into the system in unusual quantity; it is not eliminated by any of the ordinary channels; it cannot be retained

¹ *The Germ Theory of Disease*, by T. J. MacLagan (Macmillan), 1876; and *Fever: A Clinical Study*, by T. J. MacLagan (Churchill), 1888.

as water—what then becomes of it? It is consumed by the minute organisms which constitute the fever poison; it is by them and not by the tissues that it is taken up, and it is by them rather than the tissues that the nitrogen supplied by the food is also consumed; so the tissues are starved. In the muscles such action causes wasting and loss of power; in the heart, feebleness; in the skin and mucous surfaces, dryness; in the brain, wandering and delirium.

It is thus that the febrile symptoms of the malarial fevers are to be explained; the poison is reproduced in enormous quantity in the blood and consumes there the nitrogen and water of its environment, and so long as this action goes on the fever continues. What we have to explain in malarial fever is why it is intermittent.

The malarial poison grows in and at the expense of the system. It is, therefore, a parasite. It is a law of almost universal application in the parasitic world that each parasite affects its own special organ or tissue, has its own special nidus or habitat in which it is reproduced, and away from which it ceases to manifest life and activity. The parasite of ring-worm affects the roots of the hair of the head; that of sycosis the roots of the hair of the moustache and beard. The *trichina spiralis* makes its nest in muscle rather than in any other tissue. The flukeworm of sheep makes its home in the liver. In the same way the poison of typhoid fever affects the glands

of the small intestine; that of scarlet fever the skin and throat; that of measles the skin and mucous surfaces of the respiratory tract; that of relapsing fever makes a habitat of the blood. Why each of these parasites has its special habitat we do not know; but we do know for a fact that it is so, and that each parasite finds in its nidus something which is necessary to its vivification and reproduction as distinguished from its organic growth, and which it finds nowhere else. It is the existence of the nidus that leads to the localisation of each parasitic disease in a particular locality, and so gives to it one of its distinctive features—a special seat; it is its special local lesion which imparts to each of the specific fevers the distinctive features by which it is recognised. Smallpox is known by its eruption, and it is in the matter of its pustules that the poison most abounds. The distinctive feature of typhoid fever is the intestinal lesion; the affected glands are the nidus of the typhoid poison, the special seat of its vivification and reproduction; it is in the discharges which come from them, therefore, that the typhoid poison is most abundant. For the same reason the poison of scarlet fever most abounds in the discharges from the throat and in the peeling cuticle. The only one of the specific fevers which has no local lesion is relapsing fever; its distinctive feature is the relapse. It is also the only one whose poison is found abundantly in the blood. It is a contagious fever, and therefore its poison ranks with the contagia. But

though pathologically ranked with the contagious fevers, it has many clinical analogies with the malarial. It is, in fact, a sort of clinical link between the two. It ranks with the specific fevers, inasmuch as it is contagious, occurs in an epidemic form, and runs a pretty definite course ; it resembles the malarial fevers, inasmuch as it has no special local lesion ; has for its distinctive feature an intermission—a period of apyrexia between two attacks of fever ; and inasmuch as one attack confers no immunity from a second.

If we can explain why it is that relapsing fever has no local lesion, why the fever recurs, and why one attack of the disease confers no immunity from a second, we shall probably find in that explanation a clue to the explanation of similar phenomena in the malarial fevers.

These peculiarities of relapsing fever are all due to the fact that the spirilla which gives rise to it finds the material necessary to its vivification and reproduction, not in a localised organ or tissue, but in the blood. The blood is its nidus ; and the spirilla is found abundantly in the blood for the same reason that the poison of smallpox is most abundant in the matter of the pustules, the poison of typhoid fever in the discharges from the sloughing intestinal glands, and the poison of scarlet fever in the peeling cuticle and in the discharges from the throat.

The materials requisite to the organic growth of the poisons of the eruptive fevers (nitrogen and water)

exist all over the body and are practically unlimited. The special material essential to the vivification and reproduction of each poison exists only in its nidus, and therefore only in limited quantity. So long as any of it remains the poison continues to be propagated, and the febrile symptoms are kept up. When it is exhausted the necessary nidus no longer exists, the propagation of the poison ceases, and the fever comes to an end. That it is the propagation of the poison in the system and not its mere presence there that causes the febrile symptoms is proved by the fact that these symptoms come to an end, and the patient enters on convalescence while the system still contains much of the poison, as is evidenced by the facts of infection. Convalescents from typhus fever, scarlet fever, measles, etc., are a source of danger to others for some time after they have entered on convalescence. What brings the fever to an end is not the extinction or elimination of the poison, but the cessation of its reproduction consequent on the exhaustion of its nidus. Were this nidus to be renewed before the whole of the poison was eliminated, the poison would be reproduced and the febrile symptoms would recur. Such a thing is not likely to happen in the eruptive fevers, because the tissues which constitute the nidus are not capable of speedy reproduction; cuticle and intestinal glands are not likely to be formed anew. It is different in relapsing fever. Its nidus is the blood, and the blood is an ever-changing fluid constantly

being renewed, and containing nothing which is not likely, when used up, to be quickly replaced. As it is the localisation of its nidus in a special locality that gives to each eruptive fever the special lesion which forms its distinctive feature, so it is the localisation of its nidus in the blood that gives to relapsing fever its distinctive feature—the relapse. It relapses because the nidus is renewed before there has been time for the whole of the poison to be eliminated from the system.

If such be the explanation of the relapse, it is evident that cases may occur in which, either from more rapid elimination of the poison or more tardy renewal of the nidus, the poison is all eliminated before the nidus is renewed; in such circumstances there would be no relapse, the attack being completed in one seizure. That such cases do occur is an established fact in the history of relapsing fever. Of 2425 cases collected by Murchison, 724 had no relapse; of 100 consecutive cases under Murchison's own care, 4 were completed by one pyrexial attack; of 400 recorded by Litten, 6 had no relapse.

On the other hand, it is evident that the process might be repeated more than once, that a third seizure might be caused in the same way as the second, and a fourth in the same way as the third; and so it is found to be.

Of 1500 cases collected by Murchison, a second relapse occurred in 109, or in 1 in 14; a third in 9, or in 1 out of 166; and a fourth relapse, *i.e.* 5 pyrexial

attacks, in 1 of the 1500. The duration of the attacks gets shorter as they go on. In Litten's cases the mean duration of the first attack was 6·6 days

„	„	„	second	„	4·9	„
„	„	„	third	„	3·1	„
„	„	„	fourth	„	3·1	„
while that of the fifth attack was only					2·3	„

The longer the attack the greater the amount of poison reproduced. Each successive seizure is shorter than its predecessor; the quantity of poison to be eliminated at the close of the pyrexia gets less and less, so that there is after each attack an increasing chance of its elimination being completed before the nidus is renewed. It soon happens that the poison is all eliminated before this renewal takes place. The patient then enters on permanent convalescence. In time, however, the nidus is sure to be renewed, and the blood restored to its former state. One attack of relapsing fever, therefore, confers no immunity from a second.

It is with the *plasmodium malariae* as it is with the spirilla of relapsing fever; it is present in the blood during the pyrexia and absent during the apyrexia; and there is as good reason in the one case as in the other to regard the recurrence of the pyrexia as dependent upon the reproduction and reappearance of the poison, and the recurrence of the apyrexia as dependent on its disappearance. The explanation which has been given of the alternations of pyrexia

and apyrexia in relapsing fever would serve to explain the like phenomena as they present themselves in malarial fever—the fever intermitting not because the poison is destroyed or eliminated, but because the nidus on which its reproduction depends is exhausted. This nidus is the blood; it is something in that fluid, probably in its red corpuscles, that makes it a suitable nidus for the plasmodium malariae. It is something, therefore, which, if exhausted, is sure to be quickly renewed (for the blood and its red corpuscles are ever being renewed). It is renewed before the malarial poison is eliminated from the system; its renewal leads to a fresh reproduction and growth of the poison and to the recurrence of the fever; and so the process goes on, the nidus being exhausted and renewed, and exhausted and renewed again and again, and the fever recurring and intermitting, and recurring and intermitting with each recurring renewal and exhaustion of the nidus.

The distinctive and characteristic feature of malarial fever, its remitting and intermitting course, is, according to this view, to be explained in the same way as the relapse which is characteristic of relapsing fever, and as the special local lesion which characterises each of the eruptive fevers. Each fever owes its distinctive characteristic to the peculiarities of its nidus more than to the peculiarities of its poison. In all of them the reproduction of the poison in the system leads to the consumption of the nitrogen and water of the blood

and tissues, and to the phenomena of fever; but each poison has its own special and peculiar nidus in which, and in which alone, it is vivified and brought into active life. It is the seat and nature of this nidus which imparts to each form of fever the special features which characterise it, and by which it is distinguished from all the others—in typhoid fever the bowel lesion, in smallpox the eruption, in relapsing fever the relapse, in ague the intermission.

When the nidus is exhausted the fever comes to an end. The time requisite for its exhaustion varies in different fevers, and gives to each of the specific fevers one of its distinctive features—a definite period of duration. In relapsing fever the nidus is used up in about a week, in typhus fever in about two weeks, in typhoid in about three; hence the respective duration of these fevers—7, 14, and 21 days.

In malarial fever the nidus of the poison exists in the blood. No structure or tissue in the body is so unceasingly and speedily renewed as the blood is. The nidus of the malarial poison is thus ever undergoing renewal. The rapid growth of the plasmodium leads to the sudden onset of the fever; the same cause leads also to a speedy exhaustion of the nidus, and speedy decline of the fever; but the nidus is renewed with great rapidity; and so exhaustion and renewal follow each other in rapid succession, and, in the absence of treatment, for an indefinite period. Hence

malarial fevers, instead of relapsing, only remit or intermit, and go on doing so for an indefinite time, if their course is not arrested by treatment.

One point by which above all others the poisons of malarial fevers are distinguished from those of the specific fevers is, that they are not eliminated from the system in an active form. Their life-history is completed in the system. The only possible explanation is that the poison is destroyed in the system, probably in the eliminating organs; and it is not unlikely that the copious action of the skin, and the copious deposit of lithates in the urine of those suffering from malarial fever, may be in part due to the elimination by the skin and kidneys of products resulting from the destructive disintegration of the minute organisms which constitute the poison. We know from the action of quinine on them, that these organisms are readily destroyed in the system.

It is in connection with the pathogenesis of rheumatic fever that we have been led to consider the nature and mode of action of malaria. We believe the rheumatic poison to be malarial in nature. If it be so, it is a minute parasitic organism whose morbid action, like that of the *plasmodium malarie*, is dependent on its growth and reproduction in the system; and which, like all other parasitic organisms, has a special nidus which is essential to its vivification, without which it cannot enter on its disease-producing

career, and whose special seat is likely to impart to rheumatic fever, as it does to ordinary malarial fever, and to each of the specific fevers, the peculiarities which are distinctive of it. How can a poison of this nature, and having such a mode of action, cause the phenomena of rheumatic fever?

CHAPTER X

THE PATHOGENESIS OF RHEUMATIC FEVER, OR ACUTE ARTICULAR RHEUMATISM

THE phenomena which present themselves for consideration in this disease are—

(1) The occurrence, along with the general febrile disturbance, of a local inflammatory lesion.

(2) The almost entire limitation of this lesion (1) to such parts of the motor apparatus of the body as are habitually subject to active movement, and (2) to the left side of the heart.

(3) The tendency of the disease to attack those of a particular age.

(4) Its hereditary transmission.

(5) The presence in the blood of an excess of fibrine.

(6) The presence in the blood of an excess of lactic acid.

(7) The occurrence of profuse perspirations.

(8) The shifting character of the joint affection.

These we shall consider in the order enumerated.

1. *The occurrence, along with the general febrile disturbance, of a local inflammatory lesion.*

Such association occurs under two different circumstances: (1) The inflammation may precede the fever; or (2) the fever may precede the inflammation. In the former case, the fever is the result of the inflammation, and is said to be symptomatic; in the latter, its onset precedes the evidence of local inflammation, and it is said to be idiopathic. An instance of the former we have in pleuritis or synovitis following cold or injury; an instance of the latter we have in the bowel lesion of typhoid fever, and in the sore throat of scarlatina.

The first evidence of the existence of acute inflammation of fibrous or serous tissue is pain. The first evidence of febrile disturbance is a feeling of cold and *malaise*. In purely local inflammations pain is the first symptom. Shivering, *malaise*, and general febrile disturbance may quickly follow, or may even be contemporaneous with the pain; but they do not precede it. In the local lesions of the specific fevers the case is different. Before their existence can be determined, there is evidence of constitutional disturbance. In the one case, the local symptoms precede the constitutional; in the other, the constitutional precede the local. Which first show themselves in rheumatic fever? There is some variety in its mode of onset. Usually the patient complains at first only of chilliness and general *malaise*, accompanied by aching of limbs. Soon fever is decided, and the pains are localised in the joints. But one

or two days generally elapse before the joints are distinctly inflamed. In milder and subacute attacks, the local joint affection is often the first and only thing complained of; but careful inquiry nearly always elicits the fact that the patient has been "out of sorts" or has "had cold" for a day or two before the joint affection declared itself. In whatever way the malady commences, then, the joint affection is preceded by evidence of constitutional disturbance. But though this is true, it is equally the case that the fever does not reach its height till the articular inflammation is established, and that the full development of the fever is contemporaneous with the height of the joint affection. When once the disease is fully established, the local inflammation and the constitutional disturbance go hand in hand,—they rise and fall *pari passu*,—and there can be no question that the febrile disturbance, though antecedent to, is much increased by, the local inflammation. In this respect the joint inflammation of rheumatic fever resembles the local lesions of the eruptive fevers more than it does common inflammation due to a local cause.

How is the inflammation of the fibrous and serous tissues induced? That it results from the action of the rheumatic poison there can be no doubt. The question is, "How does the poison act?" It may act in one of two ways: either as a direct irritant to these tissues, causing in them the same

kind of excitation that cantharides produces in the bladder, and arsenic in the stomach and rectum; or it may act after the manner of a contagium, and owe its action on the fibrous and serous tissues to its propagation in them.

If its action were that of a direct irritant, the course of events in acute rheumatism could scarcely be what they are; for were such its mode of action, all the fibrous textures and all the joints should suffer simultaneously and in a like degree; the inflammation would either soon decline or it would become more severe, and would frequently terminate in suppuration; the heart would suffer in every case; and the small joints be as liable to suffer as the large. The gradual onset of the rheumatic inflammation, its shifting character, its uncertain course, its tendency to select certain joints, its occasionally prolonged duration, and its gradual decline, can be best explained on the view that a fresh supply of poison is constantly being brought into play; that the local as well as the general symptoms of rheumatic fever are the result of the propagation of its poison in the system; and that the rheumatic process takes place in the fibrous textures of the motor apparatus because it is in these that the rheumatic poison finds the nidus necessary to its vivification and reproduction. The joint troubles of rheumatic fever are, on this view, the necessary result of the propagation of the rheumatic poison in the structures which are the seat of inflammation, and bear

to the general febrile disturbance of that disease the same pathological relation that the local lesions of the eruptive fevers bear to their general symptoms. In the eruptive fevers the distribution of this nidus varies both in situation and extent; it does the same in rheumatic fever. In scarlatina the skin and throat are the nidus, but it is not always equally distributed between the two; when in excess in the skin there is an abundant eruption and not much sore throat; when in excess in the throat there is bad sore throat and not much rash. So in measles, the nidus has two seats—the skin and mucous surface of the respiratory tract; when concentrated in the skin, there is an abundant eruption and no serious chest complication; when concentrated in the respiratory organs, the eruption is scanty and the chest complications are serious. In rheumatic fever the nidus may exist in many joints or only in two or three; in the former case many joints will suffer, and the attack be severe; in the latter, few will suffer, and the attack be mild.

In the ordinary forms of malarial fever the poison finds its nidus in the blood; there is, therefore, no local lesion. In rheumatic fever the poison finds its nidus chiefly in the fibrous structures of the large joints; it is in these textures that its vivification and active reproduction take place; it is on them, therefore, that its morbid effects are chiefly manifested. This localisation of the nidus in a special structure imparts to rheumatic fever one of the clinical features

of the eruptive fevers—general febrile disturbance *plus* a local lesion. As relapsing fever constitutes a sort of clinical link between the eruptive fevers and the malarial, so rheumatic fever is a sort of clinical link between the malarial fevers and the eruptive. The absence of a localised nidus imparts to relapsing fever one of the characteristic features of malarial fever—the tendency to relapse; the presence of such a nidus in rheumatic fever gives it one of the features of the eruptive—a local lesion.

2. *The local inflammation is limited in the joints almost entirely to such fibrous and serous textures as are associated with active movement, and in the heart to the left side.*

The structures which go to form a highly developed joint such as suffer in acute rheumatism are: (1) the cartilaginous ends of the bones; (2) a sac of synovial membrane investing these, and reflected over the inner surface of the fibrous capsule; (3) the ligaments which bind together and prevent undue movement of the ends of the bones; (4) the tendons of the muscles which move the joints, many of which run in grooves or sheaths having a lubricating surface similar to that which exists in the joints; and (5) the muscles themselves without which the joint structures would be useless. All the structures here enumerated are necessary to the formation and functional completeness of a freely mobile joint. But they do not all equally suffer when that joint is the seat of rheumatic

inflammation. It is on the fibrous and serous structures—the muscles, tendons, ligaments, and the lining membranes of the joints and tendinous sheaths—that the action of the rheumatic poison is most manifested.

The symptoms of acute rheumatic inflammation of a joint are pain, swelling, and redness; and the more acute the case the more marked these symptoms. Pain is the evidence of inflammation of the fibrous textures. Swelling results from inflammation of, and effusion into, the sac of the synovial membrane. Redness occurs in cases in which the inflammation is sufficiently severe to cause hyperæmia of the vessels of the skin; it is therefore more common in joints like the knee and wrist, in which the inflamed structures are near the surface, than in those like the hip and shoulder, in which they are more deeply seated. When considering the question of the seat of rheumatism (Chap. III.), we saw that the muscles also participated in the morbid process. It is in them and in the fibrous ligaments and tendons that the morbid process first shows itself; aching tenderness of the limbs and pain in the joints precede swelling; and the question naturally arises whether the inflammation of the synovial membrane, instead of being primary, may not be due to the extension of the inflammatory process to it from the contiguous fibrous textures. There can be no doubt that synovial membrane is very susceptible to inflammation, and that disturbance originating in the fibrous structures of a joint readily extends to it

—witness the effusion which follows a strain. We shall by and by see reason to believe that inflammation of the lining and investing membranes of the heart is secondary to prior inflammation of the subjacent fibrous textures of that organ.

3. *The action of the rheumatic poison is confined almost entirely to those of a particular age.*

The age of liability to acute articular rheumatism is from fifteen to fifty.

This immunity of the very young and very old can be accounted for only in one of two ways: either the rheumatic poison does not enter their systems; or, having entered, it does not act. The former is a position which cannot be maintained; for there is no reason why an agency which may gain entrance to the system at twenty or thirty years of age, may not equally gain entrance at ten or sixty. The portals of the system are as free and as open at the one age as at the other. The second is a position which may reasonably be maintained; for there is distinct evidence that some poisons may under certain circumstances be introduced into the system without producing effect. We know, for instance, that a person who has not been vaccinated, and has not had smallpox, cannot be exposed to the poison of that disease without almost certainly taking it. But we also know that, having once suffered, he may be constantly exposed, and may even have the poison directly introduced into his system, without again suffering from its action. So

with each of the eruptive fevers—one attack confers, as a rule, immunity from the future action of its poison. Here we have adequate proof that a poison, and a very potent one too, may gain entrance to the system without producing any effect on it. We now note the fact in connection with the comparative immunity from rheumatic fever of the young and old, and in exemplification of the view that such immunity is due, not to absence of the rheumatic poison, but to insusceptibility to its action on the part of the tissues usually affected by it.

We have seen that the rheumatic poison acts on the fibrous and serous tissues of the motor apparatus of the body, and that its action is almost confined to the textures of those joints which enjoy a high degree of functional activity. But these textures are not equally active at all periods of life. In infancy and early life there does not exist the physical strength and stamina necessary for active movement. After the age of fourteen or fifteen matters change. The child has now reached an age at which work and vigorous exercise begin to form part of his daily life; and when adult life is reached, hard work and active exercise are of constant occurrence. This implies the constant possibility of vigorous and free movements of the larger joints, and increased force and activity of the heart's action. It necessitates, also, a state of preparedness for such action. At any time a call may be made for efforts necessitating such movement and action; and the requisite facilitating and restraining forces

must be there to meet the emergency. The period of life at which such efforts are made is from fifteen to fifty or thereabouts. This, therefore, represents the period of highest functional activity of those tissues whose function it is to facilitate and restrain movement. It also represents their period of greatest liability to the action of the rheumatic poison. The period of liability to the action of the rheumatic poison corresponds exactly to the period of functional activity of the tissues specially involved in that disease. The same thing is noted in connection with some of the eruptive fevers. It is specially marked in the case of typhoid. The intestinal glands whose inflammation constitutes the characteristic feature of that disease exist in infancy in but a rudimentary state. After two or three years, they begin to increase in size and functional activity, and go on increasing till adult life is reached. From that time till middle age they are prominent objects in the intestinal wall. They then begin to diminish in size and functional activity, and go on diminishing as age advances, till in old age they are practically non-existent, and have ceased to exercise any function. The liability to the action of the typhoid poison is directly as the size and functional activity of these glands. In infancy and old age the disease is rare. The period of greatest liability to it is from fifteen to thirty-five. All this is adequately explained on the view that these glands are the nidus of the typhoid poison and are essential to its propagation in the system.

In exactly the same way is to be explained the special tendency of the rheumatic poison to affect people between the ages of fifteen and fifty. This is the period of functional activity of those textures whose inflammation constitutes the special lesion of the disease. They form a suitable nidus for the propagation of the rheumatic poison only during their period of functional activity; it is during that period, therefore, that the liability to suffer from rheumatic fever is specially manifested.

4. *Hereditary transmission.*

Many diseases are said to run in families—to be transmitted from father to son. And the facts warrant the statement. A gouty parentage gives a liability to gout. The children of phthisical parents are in turn apt to die of the same disease. Rheumatism is also thus inherited.

But when we say that a man inherits a disease from his father, we do not mean to say that he comes into the world suffering from it, or with its seeds already in him. In the case of gout he may enjoy perfect immunity from it during the greater part of his life, and begin to suffer only when forty or fifty years of age. In the case of phthisis perfect health may be enjoyed for twenty years, and then the fatal inheritance declare itself. In the case of rheumatism, this inheritance seldom declares itself before fifteen, and is generally lost again after fifty.

The son may be born before the father has himself

suffered from the malady which he is believed to have transmitted to his offspring. Or the father may even not suffer at all; he may be simply the medium of transmission to his son of a malady from which his forefathers had suffered. Evidently it is not the disease itself but only the family tendency to it which is transmitted. To transmit an actual disease the father must have its poison in his system when his son is begotten; in which case the child will be born with the malady already developed, as in the case of syphilis. But that is a very different thing from what occurs in the case of rheumatism. What is there transmitted is not the disease, but a tendency to it—a greater or less liability to contract it.

This tendency is generally referred to as a constitutional predisposition. But to give it a name is to indictate, not to explain, its existence. What is a constitutional predisposition to rheumatism? Wherein does it consist? And what do we mean when we say that a man has inherited rheumatism from his father?

Acute rheumatism consists in inflammation of the fibrous and serous tissues of the motor apparatus. Its poison is a miasmatic organism, which is propagated in the system, and finds the nidus requisite to this propagation in those tissues whose inflammation constitutes the special lesion of the disease. For the production of acute rheumatism, therefore, two factors are necessary—first, the poison introduced from with-

out ; second, that peculiar condition of the tissues of the motor apparatus which imparts to them their special fitness to act as a nidus for this poison. Which of these factors is it that is transmitted ? or is it both ? One or both it must be, if we recognise transmission at all. It is certainly not both, for their coexistence in the system at birth would give rise to the disease in the infant. As certainly it is not the first, for a miasmatic poison is essentially one which is received into the system from without, and which gives rise to a disease which is not communicable. It can only be the second ; it can only be that peculiar condition of the tissues of the motor apparatus which renders them a fitting nidus for the propagation of the rheumatic poison. The difference between a rheumatic and a non-rheumatic subject is, that the motor apparatus of the former contains that special ingredient which is requisite to the propagation and action of the rheumatic poison ; while that of the latter does not. Between the fibrous tissues of the two men there is no difference that can be detected either by the anatomist or the chemist ; but in the one, these tissues afford a nidus for the propagation of the rheumatic poison—in the other, they do not. In the one the tissues of the motor apparatus contain something which is wanting in those of the other. It is the presence of this something which constitutes the peculiarity of the rheumatic constitution. It is the tendency to the development of this peculiarity which

is transmitted from father to son, and makes each generation susceptible to the action of the rheumatic poison. That such a peculiarity should be inherited, consists with all that we know of hereditary transmission. There is no reason why internal peculiarities should not be transmitted, as well as external—why a peculiar condition of the brain, of the stomach, of the liver, of the fibrous tissues should not be handed down from father to son, as well as a special cast of features, a particular colour of hair, a peculiar gait, or a peculiar shape of the limbs. And we know as a fact that certain peculiarities of internal organs are transmitted. Furthermore, there is no reason why peculiarities of individual structures should not descend from generation to generation, as well as peculiarities of individual organs; indeed, peculiarity of an entire organ presupposes peculiarity of its individual parts. It consists with all reason that peculiarities of the motor system should be inherited, as well as peculiarities of the nervous, digestive, osseous, and other systems of the body. That some peculiar condition of the motor system is handed down in rheumatism, we know. That this condition declares itself by a special susceptibility of the tissues of the motor apparatus to the action of the rheumatic poison, we also know. So far as the bearing of this fact on the miasmatic theory of rheumatism is concerned, we can only say that that theory perfectly consists with it.

5. *The presence in the blood of an excess of fibrine.*

In many forms of inflammation the blood contains an increased quantity of fibrine. In acute rheumatism this excess is specially marked. Fibrine was at one time believed to be an important nutrient constituent of the blood. It is now known that it is a product of tissue waste—an excrementitious rather than a nutrient compound. The evidence of this is that it accumulates during fasting, and during many ailments accompanied by increased waste. It exists also in increased quantity in the blood after fatiguing exercise; and Brown-Sequard has shown that the more a muscle is exercised by galvanism, the more fibrine does the blood issuing from it contain. There can be no reasonable doubt that fibrine is a product of the retrograde metamorphosis of nitrogenous tissue.

We know that inflammation causes increased metamorphosis of the tissue in which it occurs. We know that rheumatism consists in inflammation of the muscles and fibrous tissues of the joints. We know that these tissues are the chief source of the fibrine of the blood. We know, therefore, that rheumatic inflammation must be accompanied by increased formation of fibrine. The presence in the blood of an excess of fibrine during the course of acute rheumatism, is thus a necessary result of the morbid action which constitutes the characteristic

feature of the disease. It results from increased metamorphosis of the nitrogenous elements of muscle, just as excess of lactic acid results from increased metamorphosis of the non-nitrogenous.

6. *The presence in the blood of an excess of lactic acid.*

This, one of the characteristic phenomena of acute rheumatism, has already been considered.

It has been shown that lactic acid is a normal product of the retrograde metamorphosis of muscular tissue; that its formation in excess during muscular exercise results from increased wear and tear of the tissues of the motor apparatus; and that its excessive formation in acute rheumatism is due to the same cause, only differently induced. In the one case, the increased metamorphosis results from exaltation of a natural function; in the other, it is a consequence of a pathological process induced by the action of the rheumatic poison, and leading to excessive formation of lactic acid, in the manner already explained.

The argument may be briefly summed up as follows :—

Rheumatism is essentially a disease of the motor apparatus of the body. Acute rheumatism essentially consists in acute inflammation of the most active parts of that apparatus. The tissues chiefly involved are the muscles and fibrous textures. The rheumatic process must, therefore, be accompanied by increased

metabolism of these textures. White fibrous tissue contains only nitrogenous material; muscle contains both nitrogenous and non-nitrogenous. Its non-nitrogenous material is glucose; and it is from this that lactic acid is formed. The difficulty has been to account for the increased metamorphosis of glucose as evidenced by the increased formation of lactic acid. The view which has been advanced as to the nature of the rheumatic process disposes of this difficulty. The rheumatic poison is reproduced in the muscles and fibrous textures. By seizing on the constituent elements of these, and appropriating them in its growth and reproduction, it causes in these textures the same increased metabolism that naturally results from increased functional activity; in doing this, it necessarily causes increased formation of their ordinary metabolic products; one of the metabolic products of muscle is lactic acid. Increased formation of lactic is, therefore, one of the results of the rheumatic process; and this increased formation is kept up during the continuance of that process. It results from increased metamorphosis of the non-nitrogenous elements of muscle, just as increased formation of fibrine results from increased metamorphosis of the nitrogenous.

7. *The occurrence of profuse perspirations.*

Abnormally free action of the skin is a characteristic of acute rheumatism. As a rule, the more acute the case and the more intense the joint

inflammation, the more free is this action. The perspiration has an acid reaction, and continues during the whole course of the acute symptoms. By some, these sweats have been regarded as exhausting and debilitating, and, therefore, as injurious. By others, they have been looked upon as salutary. When two such antagonistic opinions are held, we may safely infer that neither expresses the whole truth. In some circumstances profuse perspiration is both evidence of weakness and a cause of increasing debility. In others it is unquestionably salutary, and seems to be the means by which certain disturbances of the system are brought to an end. In rheumatic fever it cannot be said to have either effect. There is no evidence that it causes such debility as results from the night sweats of phthisis; but those who study it in connection with these sweats will naturally draw the inference that it is weakening. There is no evidence that it produces the salutary effects which are noted in connection with the critical perspirations of pneumonia and other acute febrile ailments; but those who study it in connection with these critical sweats will naturally conclude that it is salutary. All cases of phthisis do not have night sweats; they are among the unfavourable symptoms of some cases. All cases of pneumonia do not have a critical perspiration; it is one of the favourable symptoms of some cases. But all cases of acute rheumatism

have acid sweats; and have them, not occasionally or at one period only, but continuously through the whole course of the fully developed disease. There is no evidence that they exercise a favourable influence on the course of the ailment; there is no evidence that they influence it unfavourably. The acid sweats of acute rheumatism are altogether peculiar—altogether different from those noted in connection with exhausting maladies, and the crisis of acute febrile ailments. They constitute one of the essential symptoms of the disease—one of the invariable results of the action of the rheumatic poison. How are they produced?

The blood in acute rheumatism contains an excess of lactic acid. This it is which gives to the perspiration its acid reaction and odour. As this acid has been regarded by many as the cause of the rheumatism, its excretion by the skin has naturally been looked upon as a thing to be desired; and this is one foundation for the belief that the profuse perspiration of acute rheumatism is salutary. For so, on this view of the matter, it ought to be. The probability is a hypothetical one, however, which is not supported by fact; for practically we find that the most profuse perspiration affords no relief to the pain. In fact the pain is, as a rule, most severe in cases in which the sweating is most free.

When considering the lactic acid theory, we saw that one of the most common and constant effects of

the internal administration of that acid was increased action of the skin. The dry and branny skin of cases of diabetes becomes under its influence moist and perspiring. If such be the effect of a comparatively small quantity given by the mouth in a disease in which there is great difficulty in getting the skin to act at all, what is likely to be the effect of its formation in large quantity in the system during the course of a malady in which there is no difficulty in getting the skin to act? Clearly profuse perspiration. That lactic acid is formed in very large quantity in the course of acute rheumatism, is evidenced by the quantity eliminated by the skin. Normally it is converted in the system into carbonic acid and water, and in that form is thrown off by the lungs and skin. The elimination of the unchanged acid indicates that there has been formed a larger quantity than can be so converted.

The profuse perspirations of acute rheumatism are due, not to an effort of nature to eliminate the rheumatic poison, but to the stimulant action on the skin of the excess of lactic acid formed during the increased metamorphosis of muscle. These perspirations are to be regarded as neither prejudicial nor beneficial; but as simply one of the essential symptoms of the disease during whose course they occur. They occupy in its symptomatology the same position as increased elimination of urea, and bear to the local lesion of rheumatic fever the same relation. The excess of

acid is the result of increased metamorphosis of the non-nitrogenous, the excess of urea the result of increased metamorphosis of the nitrogenous elements of muscle.

8. *The shifting character of the joint affection.*

This is one of the most striking peculiarities of a rheumatic attack. In the history of all forms of the disease, acute, subacute, and chronic, it occupies a prominent place; and no theory of rheumatism can be regarded as satisfactory which does not recognise and account for it.

It is impossible to explain it on any theory which recognises only the existence of a poison equally distributed through the blood, acting like an ordinary medicinal or poisonous agency, and acting, therefore, equally and continuously so long as it exists in adequate quantity.

The action of such a poison would be continuous and persistent, not shifting and variable.

The miasmatic theory, which regards the rheumatic poison as a parasitic organism, requiring for its development and action a second factor or nidus which is localised in fibrous and serous tissues, which exists in varying amount in different parts of these tissues, and which, like the nidus of ordinary malarial fevers, may be exhausted and renewed again, satisfactorily explains this peculiarity of the local lesion of acute rheumatism. Exhaustion of the nidus implies decline of inflammation, its renewal a reaccession of it.

Its exhaustion in one joint may coincide in point of time with its renewal in another. In that case the decline of the inflammation in the one will coincide with its onset in the other. In this we have the explanation of the apparent occurrence of metastasis. The inflammation seems to leave one joint and go to another; in reality it is a mere coincidence. The decline of the inflammation in the one has nothing to do with its appearance in the other; by mere accident the second factor is exhausted in the one at the same time that it is renewed in the other. With so many joints liable to disturbance, such a coincidence could scarcely fail to occur now and then. Occasionally the metastasis seems to be to the heart; but here too it is a coincidence, for in its tendency to become the seat of rheumatic inflammation the heart is in the same position as a joint.

CHAPTER XI

THE HEART COMPLICATIONS OF RHEUMATISM

THE cardiac apparatus is made up of the following structures :—

(1) The hollow muscular substance of the heart which, by its contraction, initiates the movement of the blood.

(2) Rings of white fibrous tissue which surround and form the basis of the arterial and auriculo-ventricular openings, and to which the muscular fibres are attached.

(3) Fibrinous valves whose structure is continuous with that of the rings, and whose function it is to close the various openings of the heart, to resist the backward tendency of the blood, and keep it in the proper channel.

(4) A membrane which lines the interior of the heart's cavities, and is reflected over the fibrous structure of the valves, and whose smooth surface facilitates the onward flow of the blood.

(5) An investing membrane which covers the heart externally, and whose peculiar formation and smooth

glistening surface facilitate the free action of that organ.

All these structures, with the single exception of the internal lining membrane, find their analogues in those which go to form a complete and perfect joint. They are all apt to suffer in the course of acute rheumatism, though not all to the same extent.

The function of cardiac muscle, like that of voluntary, is to initiate movement.

The function of the fibrous structures of the rings and valves, like that of the fibrous tendons and ligaments, is to afford attachment to muscle, and to regulate normal and prevent abnormal movement.

The function of the pericardium, like that of the synovial membrane of the large joints, is to facilitate free movement.

The endocardium alone has no analogue in the structures of a joint.

When considering the action of the rheumatic poison on the joints, we saw that the structures which are primarily affected and suffer most are the fibrous textures which regulate their movements—the ligaments and tendons. It is the same in the heart. The structures which chiefly suffer are the fibrous rings and valves—the structures which regulate the movement of the blood.

It is its tendency to affect the heart that imparts to rheumatism its gravest features. In the majority

of fatal cases, death is attributable to some form of cardiac inflammation.

Bouillaud was the first who insisted on the essential nature of the connection between rheumatism and this inflammation. Its frequent occurrence in the course of that disease had indeed been pointed out by others before him, notably by Pringle.¹ But it is to this distinguished French physician that we must accord the credit of having first insisted on the frequency and true nature of the heart affection. Before his time it was looked upon as a sort of metastasis, or retrocession of the inflammation from the joints to the heart. He regarded it as "one of the elements of the disease"; and as early as 1835 advocated the view that inflammation of the lining and investing membranes of the heart is of frequent occurrence in acute rheumatism, and is to be regarded as produced in the same way as the joint inflammation.²

¹ *Observations on Diseases of the Army*, by Sir John Pringle, 1761.

² "La péricardite existe chez la moitié environ des individus affectés d'un violent rhumatisme articulaire aigu. Sous ce point de vue la péricardite n'est, en quelque sort, qu'un des éléments de la maladie dite rhumatisme articulaire aigu, laquelle, considérée d'une manière plus large et plus exacte qu'on ne l'a fait jusqu'ici, constitue une inflammation de tous les tissus séro-fibreux en général, développée sous une influence spéciale. Or, le péricarde étant de nature séro-fibreuse, comme le tissu où réside le rhumatisme articulaire proprement dit, il n'est pas étonnant que la péricardite coïncide si souvent avec ce dernier : que le rhumatisme du péricarde, en un mot, ait lieu dans les circonstances qui produisent un rhumatisme des synoviales articulaires et des tissus fibreux sur lesquels elles se déploient, lequel n'est, pour ainsi dire, qu'une péricardite articulaire.

"L'endocardite, à l'instar de la péricardite, se manifeste sous les mêmes influences que le rhumatisme articulaire aigu : et bien que cette phlegmasie puisse éclater quelquefois pendant le cours d'un grand rhumatisme articulaire aigu et d'une manière purement *métastatique*, suivant l'expression de certains pathologistes, il n'en est pas moins vrai que, le plus souvent, le tissu séro-

In all forms of rheumatism, acute, subacute, and chronic, the heart is apt to suffer. In the acute, the cardiac inflammation partakes of the generally acute character of the attack, and the symptoms are well marked from the commencement. In the subacute, the symptoms are less marked, and the immediate result of the cardiac mischief less a source of anxiety. In the chronic, its onset is so gradual that the cardiac affection seldom attracts attention until it is so far advanced as to cause serious disturbance of the heart's action, and the general symptoms of cardiac disease.

The exact proportion of cases of acute and subacute rheumatism during whose course recent cardiac inflammation occurs is differently stated by different observers. And the nature of the question is such that discrepancies must exist.

In acute attacks, the heart is more apt to suffer than in subacute ; and young patients are more liable to this complication than more elderly ones. The acuteness of the attack, and the age of the sufferer, are thus important elements in determining whether or not cardiac compli-

fibreux interne du cœur se prend en même temps que celui des articulations : c'est aussi ce que nous avons vu pour le tissu séro-fibreux externe du cœur. Sous le point de vue de leur structure et de leurs fonctions, les parties du cœur qui s'enflamment par l'influence des causes productrices du rhumatisme articulaire ont la plus grande analogie avec les parties des articulations qui sont le siège de ce dernier. Les cavités du péricarde et de l'endocarde représentant, sous le rapport qui nous occupe, des espèces de cavités articulaires, il n'est pas étonnant que leurs phlegmasies coexistent si souvent avec celles des cavités articulaires proprement dites."—*Traité Clinique des Maladies du Cœur*, 1835 ; and *Traité Clinique du Rhumatisme Articulaire*, 1840. Par J. Bouilland, Professeur de Clinique Médicale à la Faculté de Médecine de Paris ; Membre de l'Académie Royale de Médecine, etc.

cations are likely to occur. An observer, the majority of whose cases are subacute, and the average age of whose patients is thirty, will have a smaller percentage of cardiac complications than one who happens to have a larger number of acute cases, and the average age of whose patients is twenty.

Fuller and others have endeavoured in studying this question to distinguish between acute and subacute rheumatism. But independently of the difficulty, nay the impossibility of drawing a distinct line of demarcation between them, there is no pathological reason for doing so. Acute and subacute rheumatism are merely different degrees of severity of the same disease.

A study of the statistics bearing on this point leads to the conclusion that we are very near the truth when we say that in the course of acute and subacute rheumatism recent cardiac inflammation occurs in about 30 *per cent*, or in nearly one case in three. But such a general statement is bald, and to some extent misleading, without the additional statement that, as years advance, the tendency to such complications diminishes.

Three facts are specially prominent in the history of rheumatic inflammation of the heart :—

- (1) It is most common in young people.
- (2) It is more apt to occur in acute than in subacute cases of rheumatic fever.
- (3) It is limited to the left side of the heart.

No theory of rheumatism is satisfactory which does not explain these very striking facts.

1. *The heart is specially apt to suffer in young people.*

This is a fact which has been observed and commented on by most writers on the subject. Dr. Peacock¹ gave it as the result of his observations on 233 cases of acute and subacute rheumatism, that of those under twenty-one years of age, 33·3 per cent suffered from recent cardiac disease; while of those over forty, only 16·6 so suffered; “showing that the occurrence of cardiac complication is much more to be apprehended in young people than at more advanced ages.” This accords with general experience. What is the explanation of it?

We have seen that rheumatism is essentially a disease of adolescence and early manhood; and that the textures which suffer most are the fibrous and serous tissues of the large joints. The tendency of a given portion of fibrous or serous tissue to be affected by the rheumatic poison is directly as its functional activity. Hence the tendency of the disease to attack the large joints. Adolescence and early manhood are the periods of life at which the functional activity of the textures which suffer is at its height. Hence rheumatism is most common in young people.

Applying the same reasoning to the case of the heart, we find in it an adequate explanation of the

¹ *St. Thomas's Hospital Reports*, vol. vi., 1875; and vol. x., 1879.

fact which we are now considering—that that organ is more apt to be the seat of recent rheumatic inflammation in young people than in those of more mature years. Muscular exertion increases the force and frequency of the heart's action. The more work the voluntary muscles are called upon to do, the greater is the demand for blood in them, and the greater the force and frequency of the heart's action. In other words, the voluntary muscles and the muscles of the heart work hand in hand; functional activity of the former necessitates functional activity of the latter. In this physiological fact we have the explanation of the pathological one which we are now considering. Rheumatism of the joints is most common in youth, because youth is the time at which these structures enjoy the highest degree of functional activity. Rheumatism of the heart is most common at the same age, and for the same reason. Sudden and rapid movements, involving correspondingly sudden and rapid increase in the force and frequency of the heart's action, are more frequent before than after the age of forty. Before that age the heart's structures are, therefore, subjected to greater and more frequent strain than they are called upon to bear in more mature years, and must be ready to meet it. With the decreasing functional activity of advancing years, comes also diminished susceptibility to the action of the rheumatic poison.

It is a *clinical* fact that the age of susceptibility

to the action of the rheumatic poison is from fifteen to fifty. It is a *physiological* fact that the tissues on which that poison acts have a higher degree of functional activity during the earlier than during the later years of that period. It is a *pathological* fact that the tendency of a given portion of fibrous tissue to be affected by the rheumatic poison is directly as its functional activity. It follows that the textures of the heart ought to be more subject to rheumatic inflammation in youth than they are in more mature years. And all observation shows that they are so.

2. *Inflammation of the cardiac structures is more common in acute than in subacute attacks of rheumatism.*

What is an acute, and what a subacute attack ?

An *acute* attack is one in which the rheumatic inflammation is both extensive and severe ; affecting several joints, and affecting them smartly. In other words, it is a rheumatic attack occurring in one in whom the rheumatic constitution is very marked ; in the fibrous tissues of whose motor apparatus the nidus requisite to the reproduction and action of the rheumatic poison is abundantly and widely distributed ; and on whom, therefore, that poison exercises a very decided action. The more abundant and wide the distribution of the nidus, the more likely is it to exist in the heart as well as in the

joints, and the more likely is the heart to be affected. As a result of its abundance, the inflammation of the individual joints is severe; as a result of its wide distribution many joints suffer. There are fifteen common seats of rheumatic inflammation—fourteen in the joints and one in the heart. The wider the distribution of the nidus, the larger the number of these seats likely to suffer at one time. In this respect, the heart is in the same position as a joint; so that the wider and more abundant the distribution of the nidus, the more likely is that organ to suffer. The same circumstances which make a rheumatic attack acute and severe, tend also to give rise to heart complications; and thus is explained the fact that such complications are most apt to occur in acute cases. The heart suffers in such cases for the same reason that a large number of joints do. Given a severe and acute rheumatic attack, during whose course ten of the fifteen common rheumatic centres are affected—the heart is more likely to be among the ten which suffer than among the five which escape; the chances are two to one against it. Given a mild and subacute attack, during whose course only five centres are affected—the heart is more likely to be among the ten which escape than among the five which suffer; the chances are two to one in its favour.

The effect of age in increasing and diminishing the danger to the heart, we have already considered.

The influence of these two agencies—the age of the sufferer, and the severity of the attack—ought to be considered conjointly; for severe attacks of acute rheumatism seldom occur except in youth; and nearly, if not quite, always in youth for the first time. It is probable that the severity of the attack has, in the manner just explained, as much to do with the production of the heart affection, as has the youth of the sufferer.

The rheumatic constitution is not acquired, but natural—maybe inherited. A man who has it can scarcely reach the age of forty in a temperate climate without suffering from rheumatism; and he is more likely to suffer for the first time between the ages of twenty and thirty than between thirty and forty—and that simply because the former decade comes first. If his constitution be a markedly rheumatic one, he will suffer severely, and the majority of his rheumatic centres will be affected. The heart is more likely to be in the majority which suffer than in the minority which escape. That organ suffers, therefore, not so much because the man is young, as because his constitution is a markedly rheumatic one; and because exposure to the rheumatic poison is too common to permit of the likelihood of his getting beyond youth without suffering from its action.

That the rheumatic constitution is less marked after middle age has already been seen. This involves diminished susceptibility to the action of the rheumatic

poison ; and this diminished susceptibility is common to the whole of the structures affected in rheumatism, those of the heart as well as those of the joints.

3. *Rheumatic inflammation of the heart is limited to the left side.*

In considering the action of the rheumatic poison on the joints, we saw that those which suffer most are the ones which enjoy the highest degree of functional activity, and are habitually subject to free and active movement—the large joints. That is what clinical observation demonstrates in the case of the joints. It demonstrates the same thing in the case of the heart. The muscles, the valves, the fibrous rings, the lining and investing membranes are, as regards structure and function, the same on the right as on the left side ; only on the right side they have a less degree of functional activity ; the muscular walls are thinner and less vigorous, and the valves contain less tendinous material. These structures are thinner and weaker on the right side because they have less work to do and less strain to bear. The difference between the two sides of the heart in this respect is evidenced by a reference to the contractile force of each ventricle. The walls of the left ventricle are much stronger and thicker than those of the right ; “ the proportion between them in this respect being as three to one.”¹

¹ Quain's *Anatomy*.

It follows from this that the left ventricle acts with three times the force of the right; its fibrous structures and valves have therefore to bear three times as much strain, and enjoy a correspondingly higher degree of functional activity. "The work done by the right ventricle may be set down as one-third of that of the left."¹

The fibrous structures of the right side of the heart thus bear to those of the left the same relation that the fibrous structures of the small joints bear to those of the large; they have not the same degree of functional activity, and are not called upon to do so much work. For that reason they are not acted on by the rheumatic poison—as is demonstrated by the rarity of acute articular rheumatism in childhood, by its rarity after the age of fifty, and by the rarity with which it affects the structures of the small joints. A certain degree of functional activity, such as is got only in the large joints, and even in these only during their period of highest functional activity, is essential to the action of the rheumatic poison. This degree of functional activity, though it exists in the left side of the heart, is not attained by the structures of the right side; hence they do not suffer from rheumatism. The right side of the heart escapes for the same reason that the joints of the toes do.

Rheumatic inflammation of the heart is generally

¹ M'Kendrick's *Physiology*.

described as occurring under the three forms of endocarditis, pericarditis, and myocarditis—inflammation of the lining membrane, inflammation of the investing membrane, and inflammation of the muscular substance. For clinical purposes this is as convenient a classification as could be adopted.

CHAPTER XII

ENDOCARDITIS

By the endocardium the anatomist means the thin transparent membrane which lines the interior of the cavities of the heart; is reflected over its valves and muscular folds; is continuous, on the left side, with the lining membranes of the aorta and of the pulmonary veins; and, on the right, with those of the pulmonary artery and systemic veins.

The clinical observer attaches to the term a wider meaning, and includes under it all the structures which lie inside the heart—the fibrous rings and valves, as well as the lining membrane. It is of importance that this distinction should be borne in mind; for we shall presently see that the endocardium of the anatomist, the lining membrane of the heart properly so called, is probably never the primary seat of rheumatic inflammation. We now use the term in its wider sense. By endocarditis we mean inflammation of any or all of the non-muscular structures situated *inside* the heart—the

fibrous texture of the rings and valves, as well as the lining membrane.

Rheumatic inflammation never affects the whole surface of the lining membrane of the heart. It is almost entirely limited to the part which is reflected over the valves. When other parts suffer, the mischief is almost invariably attributable to mechanical injury produced by the rubbing on the affected portion of the endocardial surface of an already damaged valvular segment. Moreover, the inflammation does not affect the whole valvular surface; only one side of a segment suffers—that, namely, which comes in contact with another segment in the act of closure,—in the aortic valve, its convex surface, and in the mitral, its auricular. The damage is further limited in its early stage to the line at

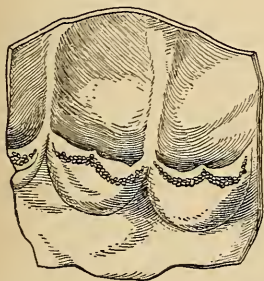


FIG. 1.—*Inflammation of Aortic Valves.*—The earlier stage of the process. Showing the situation of the inflammatory granulations.

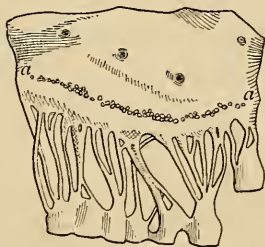


FIG. 2.—*Inflammation of Mitral Valve.*—The earlier stage of process. Valve seen from the auricular surface. Showing the situation of the inflammatory granulations.

which the segments come into contact. This is well shown in Figs. 1 and 2.

The limitation of the disease to this particular part

of the valve has been attributed to the fact that it is the part which is most exposed to friction. "In its earliest stages it always occurs near the edges of a valve in the formation of a line of little elevations along the contact line of its segments, where the friction is greatest."¹

"It is those portions of the valve which come into contact in the act of closure, and are thus most exposed to friction, which are especially involved, and in which the changes usually commence."²

That friction may produce inflammation of the lining membrane of the heart, there can be no doubt. Occurring in other than its valvular portion, it is almost always due to the rubbing on its surface of a damaged valve. Knowing this to be the case,—and finding that inflammation of its valvular portion commences at the line of contact of the different segments of the valves, and therefore at the point at which, if anywhere, they must rub,—we cannot fail to see that there is good reason for the belief that friction plays an important part in the production of the inflammation of the lining membrane of the heart's cavities which is found in connection with acute rheumatism. Were this lesion the direct result of the action of the rheumatic poison, it would not be limited to one side of the valve; it would affect both.

¹ *Lectures on Pathological Anatomy*, by Samuel Wilks, M.D., F.R.S., and Walter Moxon, M.D., F.R.C.P.

² *An Introduction to Pathology and Morbid Anatomy*, by T. Henry Green, M.D., F.R.C.P.

Furthermore, its invariable limitation to the points at which the valvular segments come in contact, shows that the cause which gives rise to it is something which comes into play only at that point. Friction is the most probable if not the only possible cause, and as the lesion is limited to the only point at which friction can come into play, the conclusion is forced upon us that friction is the direct cause of the lesion.

But the question arises—Why is there friction? Why do the segments of the valves rub against each other? When a valve is already damaged or roughened, it is easy to see how further damage may be done; but in a smooth uninjured valve how is the mischief set agoing? It cannot be that the valves constantly and naturally rub against each other—for in that case, if friction produced endocarditis, no one would be free from it; rheumatic and non-rheumatic subjects would equally suffer, and a smooth healthy valve would be the exception.

For the segments of the valves to come in contact is natural; but contact does not imply friction. Healthy valves normally come into firm and close contact, without in any way rubbing against and irritating each other; and this all the valves of the heart do 70 times every minute—100,800 times every day, 36,792,000 every year—and yet there is no evidence of friction or irritation, until suddenly some day, after this smooth action has gone on uninterruptedly at this rate for maybe twenty-five years, and

after the segments of each set of valves have, without injury and without rubbing, come into close and direct contact more than nine hundred millions of times (919,800,000), suddenly some day, the rheumatic poison gains entrance to the system, and the smooth working of the valves comes to an end—they begin to rub; the friction gives rise to irritation and inflammation of the surface of the valve, and the symptoms and signs of endocarditis are developed. How is this? How can the rheumatic poison cause the segments of the valves to rub against and irritate each other? That they do rub is undoubted. That the rheumatic poison is the cause of the morbid change is equally undoubted. The question which we have to consider is how the friction is produced.

If the inflammation of the endocardial covering of the valve be the result of friction—and there is no reason to doubt that it is so; and if this friction be a result of the action of the rheumatic poison on the valve—and there is no reason to doubt that such is the case—there must be a stage of the valvular lesion, some change in the structure of the valve, which not only precedes the roughening of its endocardial covering, but precedes and gives rise to the friction which causes this. The friction causes roughening, but what causes the friction?

Structurally a valve consists of two folds of the endocardium enclosing between them the fibrous or tendinous material which imparts to the valve its

strength, its capacity to resist the pressure of the blood, and to perform the function which it is intended to fulfil. In endocarditis the inflammation must commence in one of these structures, for there is no other structure to be affected; and there is good reason to believe that the mischief commences in the deeper-seated fibrous structure of the valve, and involves its endocardial covering only secondarily.

We have already seen that the rheumatic poison acts chiefly on those fibrous structures which enjoy the highest degree of functional activity; and that for this reason the large joints suffer more than the small, and the valves of the left side of the heart more than those of the right. The part of the valve which fits it for the work it has to do, and imparts to it its strength and its capacity to resist pressure, is not the endocardial covering, but the fibrous structure which that encloses. This fibrous structure is the main seat of functional activity; for that reason it is the part of the valve on which we should expect the rheumatic poison to act primarily and chiefly. And so it is found to be. The stage of rheumatic endocarditis which not only precedes the evidence of roughening of the endocardial covering of the valves, but also precedes and gives rise to the valvular friction which causes that roughening, is the stage of inflammatory thickening of their subjacent fibrous texture. The earliest change which takes place in this texture as a result of the inflammation consists in multiplication of its cellular

elements. This is the first and earliest result of the action of the rheumatic poison on the valve.

Rheumatic endocarditis then consists primarily and essentially of inflammatory thickening of the fibrous structure of the valves and rings, either or both ; and the changes which take place on the endocardial covering of the valves are consequent on this thickened and swollen condition of the fibrous structure. Let us see how this explains the changes found in the individual valves. First as to the aortic.

A segment of the aortic valve consists of a duplicature of the endocardial lining membrane, enclosing within it the fibrous structure. At the centre of its free border is an elevated fibro-cartilaginous nodule—the *corpus Arantii*. Bands of fibrous tissue stretch across the valve to this nodule, from the border of valvular attachment to the aortic ring. Some of these run along its free surface. Others spread out over the body of the valve, and come to a point, as it were, at the corpus Arantii. Between the fibres of the free margin, and those of the body of the valve, there is, on each side of the nodule, a small space over which no fibres run. This space, called the *lunula*, consists simply of a duplicature of the endocardial lining. It is the thinnest part of the valve. In the act of closure, the three segments of the valve are thrown together into the middle of the aortic outlet, and the three corpora Arantii come into contact at its centre. The three lunulæ also come into contact, and are firmly

pressed against each other by the aortic column of blood. They are all equally pressed down by this column; but the pressure thus exercised on each individual segment is counterbalanced by the counter-pressure on its other side of the two remaining segments. Thus this thin portion of the valve is freed from strain; for the greater the pressure of the blood column, the more perfect is the contact of the lunulæ, and the greater the counter-support which they give each other. The part on which the strain falls is the thicker fibrous portion of the valve which bounds the lunula below. The strain begins where the counter-pressure of the opposing segments ceases. "The force of the reflux is sustained by the stouter and more tendinous part of the valve."¹

This stouter and more tendinous part it is which suffers in acute rheumatism. The lunula is not affected. The granulations which are formed on the surface of the endocardial lining in the earlier stage of inflammation of that membrane, are limited to the convex surface of the line of fibrous tissue which passes from the attached border of the valve to the corpus Arantii, and which bounds the lunula below (Fig. 1). This band is at once the lowest part of the seat of valvular contact and the highest part of the seat of valvular strain. Above it there is no strain; below it there is no contact. It is the chief seat of strain and of functional activity, therefore its fibrous tissue is the seat of

¹ Quain, *op. cit.*

rheumatic inflammation. It is the lowest line of the seat of contact, therefore its endocardial covering is the seat of friction, when rendered unduly prominent by thickening of the subjacent fibrous tissue.

In the mitral valve there is no lunula; the whole structure is equally strained; and no one part is weaker than the rest. A weak point would be very liable to give way, for the strain on this valve is both greater, and more equally diffused over its surface than is the strain on the aortic. In the case of the aortic valve there is only the blood pressure to be resisted; but in the case of the mitral there is both the blood pressure and the strain of the tightened chordæ tendineæ. The whole valve may be the seat of inflammatory thickening; but the evidence of inflammatory change in the endocardial lining membrane is limited to the auricular surface, and to the line of contact of the valvular segments (Fig. 2). In other words, in the mitral as in the aortic valve the granulations are formed at that line which is at once the seat of strain and the point of contact. It is the seat of strain, therefore its fibrous tissue is the seat of rheumatic inflammation. It is the point of contact, therefore its endocardial covering is the seat of friction, when rendered unduly prominent by inflammatory thickening of the subjacent fibrous textures. Normally a valve is so perfectly adapted to the size of the orifice which it is intended to close, that, in the act of closing, its segments come into perfect and firm contact without any friction. They are

firmly pressed against each other, but they do not rub. But if the segments be thickened, it is evident that they must come in contact sooner than they ought. The size of the orifice to be closed being unchanged, and the force which closes it remaining the same, these thickened segments must come in contact before the closing force is expended. The continued operation of that force, after the segments of the valve are in full contact, must lead to further movement of the segments. Normally their movement is completed at the moment of perfect and close contact ; but here it is continued for an appreciable time after that event—with the necessary result of causing the valvular segments to rub against each other at the point of contact.

To put it otherwise. The swelling of the deeper fibrous textures of the valves necessarily elevates and makes more prominent the superficial covering of the swollen part. As the segments of the valve close, the unnaturally prominent endocardial covering of each comes into abnormally early contact with the opposing segment. The continuance of the act of closure, and therefore of valvular movement, after such contact is complete, necessarily causes these elevated surfaces to rub against each other. This friction produces irritation and inflammation of the endocardial coating of the valves at their line of contact.

The point is that the primary action of the rheumatic poison on the valves is to cause thickening of their deeper fibrous structure, and that the roughening of the

endocardial surface is a consequence of this, and not a direct result of the action of the rheumatic poison on it.

The morbid changes which take place in acute rheumatic endocarditis are as follow :—

1. There is multiplication of the cellular elements of the fibrous structure of the valve.

2. As a consequence of this, these fibrous structures are thickened.

3. As a result of this thickening, there is undue prominence of the endocardial covering of the valve.

4. As a consequence of this, the surfaces of the valvular segments come into contact before the act of closure is completed.

5. This causes them to rub against each other during the latter stage of this act.

6. The friction thus produced causes irritation and roughening of the surface of these valvular segments at the point at which they rub.

7. This roughening it is which produces the physical signs of endocarditis.

It will be seen from this that the change in the endocardial lining membrane which causes the physical signs by which we diagnose endocarditis is a comparatively late stage of the lesion ; that the earlier changes in the valve give rise to no physical signs ; and that the disease, therefore, exists for some time before it can be diagnosed. It is important to bear this in mind when considering the action, curative and prophylactic, of remedial agents.

Microscopic examination of the affected portion of valve confirms this view of the nature and seat of the morbid change. On making a section of one of these granular nodules, and submitting it to such examination, it is found that the seat of swelling is the deep layer of fibrous tissue, and that the superficial lining of the valve is merely raised up by the multiplication of the cellular elements of the subjacent fibrous texture. "If a valve with these nodules be cut for the microscope across the plain of its curtain, so as to show a section down through one of the small nodules, this will be found to be composed of a simple cloudy swelling of the tissue of the valve through a multiplication of the cellular elements in its fibrous structure, which here and there by its excess raises the surface into a little hillock. If the hillock takes the form of a distinct projecting grain, you will always find on the top of it a cap of fibrine separated from its substance by a line which the microscope defines very clearly. This cap of fibrine differs in composition from the hillock itself, though the difference is more easily seen than described, for the organisation in both is very low; but the fibrine is almost structureless, while the hillock of swollen valve substance shows the regularly placed nuclei of fibrous tissue"¹ (Fig. 3).



FIG. 3.—*Acute Endocarditis*.—A granulation from the mitral valve, showing a fibrinous coagulum upon the surface of the granulation. $\times 10$ (Rindfleisch).

¹ Wilks and Moxon, *op. cit.*

The cap of fibrine here described is fibrine which is deposited directly from the blood on the roughened surface of the endocardium, just as it would be deposited around any foreign body. The true seat of the inflammation is the deeper fibrous tissue of the valve.

When rheumatic inflammation attacks the fibrous rings, it produces there the same multiplication of the cellular elements and the same thickening as it causes in the valves; but thickening of the fibrous texture of the rings is not so serious, as it causes no such rubbing as occurs when a valve is thickened; the endocardial lining is, therefore, not at all affected, and there is no roughening of the surface. The sole result is some thickening of the fibrous ring, and possible narrowing of the cardiac orifice, which may be sufficient to cause stenosis enough to produce a murmur—at the base systolic, at the apex presystolic. As has been pointed out by Dr. Sansom, inflammation affecting the rings is sometimes accompanied by reduplication of the heart's sounds. This is probably due to some extension of the inflammation from the rings to the muscular substance in their neighbourhood. That such extension does occur there can be little doubt, as we shall see when considering the subject of myocarditis.

Rheumatic endocarditis then is primarily and essentially a disease of the fibrous structures of the heart. It is, therefore, limited to that portion of the endocardial contents in which these structures exist.

The small portion of the lining membrane of the heart which covers the fibrous valves very frequently suffers ; the much more extensive portion which lines the heart's cavities remains unaffected. The sole difference between the two is that the one is, and the other is not, in direct contact with the fibrous textures, and that the one is, and the other is not, the seat of friction when these textures are inflamed and swollen.

The lining membrane of the heart differs in structure, in nature, and in function, from that which invests it externally. Error and misconception have arisen from not recognising this, and from regarding endocarditis as bearing to the endocardial lining membrane the same relation that pericarditis bears to the pericardial investment. There is little or no analogy, either physiological or pathological, between the two membranes. The function of the endocardial lining is, by presenting a smooth surface to the blood, to facilitate its onward flow. It has exactly the same part to perform as the lining membrane of the arteries, with which it is structurally continuous. Neither in the heart nor in the arteries does this membrane tend to take on inflammatory action ; and when inflammation does occur in it, it shows no tendency to spread. The irritation produced by the rubbing of a valvular vegetation against the lining membrane of the ventricle, may be so great as to cause ulceration at the point of contact ; but the mischief is limited

to this point, and does not spread. There is no such disease as acute general rheumatic inflammation of the endocardium. The membrane has no vessels, and inflammation cannot spread over its surface as it does over that of the vascular pericardium.

The symptoms and signs of rheumatic endocarditis vary with the seat of the disease and the severity of the attack. Occurring, as it does, in the course of acute rheumatism, any febrile disturbance to which it may give rise is apt to be lost in that attributable to the joint inflammation. That endocarditis slightly raises the temperature, there can be no doubt, but the invasion of fresh joints has a more marked effect in that way, and as the cardiac complication generally occurs at a stage of the illness when fresh joints are apt to suffer, it is seldom possible to say how much of the abnormal rise is due to the heart affection. Inflammation of the endocardium may cause less general disturbance than inflammation of a joint; while its local effects may be so slight as to be imperceptible to the patient.

The symptoms special to it are subjective and objective. The subjective are not commensurate with the serious nature of the ailment. They vary with the severity of the attack. Frequently they are altogether absent. In very acute cases there may be pain in the cardiac region, the heart's action may be disturbed and rapid, the breathing accelerated, oppressed, or even laboured, and the patient very

anxious. If both aortic and mitral orifices and valves are acutely inflamed, such are apt to be the symptoms. But in such acute cases the muscular substance of the heart is generally more or less involved in the inflammatory mischief, and it is probable that some of the symptoms are due to this, as much as to the endocardial inflammation. Moreover, the pericardium is also liable to be inflamed in such severe cases.

When the inflammation is less severe, and is limited to the endocardium, there may be no more than a sense of uneasiness in the region of the heart, with little or no disturbance of the breathing, or of the cardiac action. In many cases, subjective symptoms are entirely absent; and the sole indication of the existence of the endocarditis is the altered character of the heart's sounds—the alteration generally consisting in the development of one or more murmurs.

It has been said that such murmurs may be of anæmic origin. I do not think that nowadays they ever are so. They may sometimes have been so in the old days of free bleeding; but in the absence of such treatment, an anæmic murmur is not likely to be developed in the short time that suffices for the production of those which we are now considering. In acute rheumatism an anæmic murmur could scarcely be developed till late in the case; those now under consideration generally appear in the early stage of the disease.

In the aortic valve we have seen that the morbid

change consists in thickening of its segments, and in roughening of their convex surfaces (Fig. 1). During the systole of the heart these segments are thrown against the walls of the aortic outlet. Thickening of their fibrous texture must, therefore, cause a diminution of the calibre of this outlet—a diminution which is directly as the extent of the morbid change; while the deposition of fibrine on the surface of the valve, not only further diminishes the aortic outlet, but, by presenting to the blood a roughened surface, interferes with the naturally smooth and easy passage of that fluid from the heart into the great vessels. The result and the physical evidence of this state of matters is the development of a systolic murmur loudest at the base, and transmitted into the aorta. If one or more of these segments should be so altered as to render due closure of the valve impossible, some of the blood regurgitates back into the ventricle from the aorta, and there is developed a diastolic basic murmur, transmitted downwards into the heart, and most distinct at mid-sternal region.

Thickening of the fibrous structures of the heart is not limited to their valvular portion; the rings also suffer. The effect of this on the aortic ring is still further to diminish the calibre of its outlet, and increase the signs of aortic obstruction.

In the mitral valve the morbid change consists in

thickening of its structure, and in roughening of its auricular surface at the line of contact of its segments (Fig. 2). Such morbid change in the mitral valve is apt to produce more serious disturbance of the valvular function than does a corresponding change in the aortic. For in the aortic the thickening is partial; the lunulæ are not affected; and so long as they come well into contact the valve continues to perform its function.

But in the mitral valve there is no lunula; the whole segment is thickened. This means loss of mobility, loss of pliability, and consequent loss of adaptability—a condition which is exaggerated by the roughening of the surface of the valvular segments at their line of contact. The result is that the two segments do not come into close and perfect contact, a certain quantity of blood regurgitates back into the auricle, and there is developed a mitral systolic murmur. Should the fibrous ring be sufficiently thickened to cause narrowing of the mitral orifice, there will be developed a presystolic blow, the evidence of mitral obstruction.

Thickening of the rings gives rise to no friction and no roughening of the endocardial surface, and is for this reason more often recovered from than thickening of a valve.

The absence of pain in rheumatic inflammation of the fibrous textures of the heart is one of the chief points of distinction between it and similar inflammation of the fibrous textures of the joints.

Another distinction, and one of much more serious import, is that the results of rheumatic inflammation of the textures of a joint are generally transient and perfectly recovered from; while those of like inflammation in the textures of the heart are apt to be permanent. Why is this? The poison which produces the inflammation is the same in both. The tissue on which it acts has in each the same structure and a similar function. Why, then, should the results be so different?

The temporary character of the injury to the textures of the joints has been ascribed to the absorbent effects of the pressure exercised on the effused products by the surrounding solid structures. The permanence of the damage to the textures of the heart has been ascribed to the absence of such pressure. "The permanence of the injury in the case of endocarditis is simply due to the want of counter-pressure. In the joints the swollen membranes are pressed against the other solid structures as soon as the liquid effusion is removed. This pressure causes absorption of all the new products, whereas in the heart there is no direct pressure of solids against the inflamed valves, which stand freely in fluid blood, so that the new products persist."¹

A more probable and adequate explanation of this unfortunate difference is to be found in the fact that when the fibrous textures of a joint are inflamed they

¹ Wilks and Moxon, *op. cit.*

get perfect rest, and are thus placed in circumstances favourable to complete recovery; while the fibrous textures of the heart not only get no rest, but from the greater frequency of the heart's action, are called upon to do an increased amount of work. They are thus placed in circumstances which make complete recovery all but impossible.

Acute cases of rheumatism, in which the textures of the joints are smartly inflamed, in which there is a considerable amount of thickening and effusion, and in which complete rest is given to the inflamed textures, are also those in which these textures are most fully and speedily restored to their natural state. In chronic cases in which the inflammation is slight, in which the patient continues to go about, and in which, therefore, the inflamed ligaments and tendons do not get rest, these textures are more apt to be permanently thickened. If pressure were the agency which removed the effusion, it ought to disappear more speedily in these chronic cases than in the acute; for the act of locomotion supplies this factor, and would lead to speedy absorption of the effused products, and early restoration of the fibrous textures to their normal state. The long duration of the thickening and stiffness of the joints in such cases is to be explained in the same way as the persistent nature of the cardiac damage. Absence of rest leads to imperfect recovery and permanent injury.

It is difficult for a heart whose fibrous textures

have once been thickened by inflammation, and whose endocardial lining has once been roughened, to recover its normal condition. For the fibrous textures continue to be strained, and the roughened surfaces of the segments go on rubbing. Irritation is thus kept up after the primary inflammation has disappeared; the thickening of the fibrous textures becomes chronic and permanent; and fresh rheumatic attacks may add to the mischief. With the advance of time the morbid change is apt to become more marked; the valvular segments to become contracted and misshapen; the cardiac circulation to be more disturbed; the muscular walls of the heart to hypertrophy, and its cavities to dilate; and so the sufferer enters on a prolonged course of misery, whose only termination is death.

It seems a simple statement of fact, clinical and pathological, to say that in rheumatic inflammation of a joint complete recovery is the rule, while in rheumatic inflammation of the heart complete recovery is the exception. The statement is one which nearly every physician would endorse. Nevertheless, it is not strictly accurate. It is bald, and misleading from its baldness. Everything which recovers in a joint may, and frequently does, recover in the heart. The structures in the heart which are apt to be permanently damaged are the valves, and these have no analogue in a joint. The pericardium corresponds in structure and function to the synovial membrane. The muscles of the heart have their analogue in the

muscles of the limbs; the fibrous rings resemble in structure and function the fibrous attachments of muscles. The valves alone have no analogue in a joint; there is absolutely nothing in or about a joint which at all resembles them either in structure or function. The changes which take place in them during the course of acute rheumatism do not result from the direct action on them of the rheumatic poison, but are produced by rubbing of the valvular segments consequent on rheumatic inflammation and thickening of the subjacent fibrous structure of the valves. Such an action cannot occur in any joint structure.

The difference in the ultimate results of rheumatic arthritis and rheumatic endocarditis is due to the different conditions of the inflamed textures.

1. An inflamed joint gets complete rest, and is thus placed under conditions most favourable to recovery. An inflamed heart not only gets no rest, but beats more quickly than natural.

2. The structures in the heart which are the chief seat of permanent damage, the cardiac valves, do not exist in a joint, and bear no resemblance to anything that does.

3. The main agency which produces and keeps up the valvular irritation—friction, the rubbing against each other of the irritated surfaces—is one which does not operate in a joint.

Though lasting damage to the heart is a frequent

result of rheumatic inflammation, it is not inevitable or invariable. In the old days the rheumatic process lasted so long in the heart, as in the joints, that its effects were seldom perfectly recovered from. Nowadays we have in the salicyl compounds so certain a means of arresting the rheumatic process that the cardiac mischief is less apt to be prolonged, and the resulting damage less apt to be irremediable. I have seen not a few cases in which the physical signs of valvular damage have entirely disappeared, leaving no trace behind—persistence in the salicyl treatment and absolute rest being the only remedies employed.

CHAPTER XIII

PERICARDITIS

BETWEEN the pericardium of the anatomist and that of the pathologist there is no difference. Rheumatic pericarditis consists in rheumatic inflammation of the investing membrane of the heart. As already explained, such inflammation is most common in acute cases, and in young subjects.

Of all the serous membranes of the body the pericardium is the only one which invests an organ having free and active movements. So far as functional activity is concerned, the pericardium is as much above other serous membranes as the valves of the left side of the heart are above those of the right, and the fibrous tissues and serous linings of the large joints above those of the small.

Pericarditis occurs in different degrees of severity. The whole membrane may be the seat of acute inflammation, or only a small part of it may be affected. According to its extent and severity are the symptoms to which it gives rise. As a rule, subjective symptoms are more marked than in endocarditis.

In acute and severe cases pain in the region of the heart is generally present at the outset, and is often the first thing complained of. Usually it is increased by pressure over the heart, or in the epigastrium. The patient is restless and distressed; his countenance has an anxious expression; the breathing is quickened; there is generally a short frequent cough; the heart's action is vigorous and rapid—maybe tumultuous, violent, and irregular. On auscultation there is heard the friction sound produced by the rubbing against each other of the roughened pericardial surfaces.

But the heart symptoms are not always so distinct in these acute cases. Occasionally their place is taken by nervous symptoms so marked that the case is apt to be mistaken for one of cerebral rheumatism. The onset of the pericardial inflammation may be ushered in by delirium; and delirium, stupor, and coma may be its characteristic symptoms throughout. From beginning to end there may not be a single subjective symptom of cardiac disturbance.

The following case, recorded by Andral,¹ is a good illustration of the manner in which acute pericarditis may simulate inflammatory mischief in the nervous centres:—

“Symptoms of Meningitis. Acute inflammation of the pericardium.”

“A woman, aged 26, the mother of two children, and who had recently had a miscarriage, was

¹ Andral, *Clinique Médicale*, tome i. p. 34.

admitted into la Charité early in the year 1820, in such a state of delirium that no information could be got regarding her antecedents. The delirium was remarkable for the obstinate taciturnity by which it was accompanied. When asked a question, the patient looked fixedly at one without answering; the face was pale; the lips, separated from each other, and agitated from time to time as by a convulsive trembling, allowed the tongue to be seen, moist and white. The pulse was frequent and small, but regular; the skin rather cold. During the next two days there was frequent bending backwards of the head, sudden raising of the trunk at intervals, and *subsultus tendinum*. The patient spoke, and appeared to understand what was said to her, but was quite incoherent in what she said. The face was very pale; the pulse very frequent and intermittent. On the fourth day after admission the delirium ceased; the patient complained only of great weakness; the muscles of the face were agitated by almost continual convulsive movements; and the upper extremities were affected from time to time with an almost tetanic rigidity. On the fifth day the delirium returned, the features were distorted; during the course of the day the patient became comatose, and died in the evening."

On *post-mortem* examination it was found that "there was no appreciable change in the colour or consistence of the brain, spinal cord, or their membranes. The digestive canal, opened throughout its

whole extent, presented only a slight injection here and there. The other abdominal viscera were free from lesion. The lungs were slightly congested posteriorly. The substance of the heart presented no trace of morbid change; the vessels entering and issuing from it were also healthy. But the pericardium was covered with a lymph deposit (*par des concrétions albumineuses*), which stretched at many points like a soft bridle from the visceral to the parietal surface. Effused into its cavity, too, were several ounces of a greenish and flocculent serum."

In subacute pericarditis the subjective symptoms are less marked. There may be no more than a sense of uneasiness about the heart, with some increased rapidity of its action. In some mild cases there are no subjective symptoms whatever—nothing but the pericardial rub to point out the existence of the disease. In not a few the inflammation is limited to that portion of the membrane which surrounds the great vessels at the base of the heart, and may give rise to no symptoms, either subjective or objective. In the *post-mortem* room this very limited form of the malady is often found in those who have died of some other complication.

The earliest stage of inflammation of the pericardium consists in hyperæmia of the membrane. It cannot be said that this stage has any specially characteristic symptoms or physical signs. But in acute

cases it is accompanied by increased vigour and energy of the heart's action. Without producing any bruit, this increased vigour imparts to the first sound of the heart an exaggerated ring or tone, which may be sufficiently marked to enable us to suspect, if not actually diagnose, commencing inflammation of the pericardium. This "tension sound," as it has been called, may be regarded as the earliest objective evidence of the onset of pericarditis. It is only in acute cases that it is observed; and in them the first stage of the disease, during which alone it is heard, lasts for so short a time that this sign may readily escape detection. When observed, it is soon thrown into the background by the more striking and important indications of the following stage.

The second stage comes in quick succession to the first. It is characterised by the effusion of lymph, and the formation of a fibrinous layer of new material, on the surface of the inflamed membrane. It is at this period that the signs and symptoms of the disease come to the front, and that its existence is generally diagnosed. The new material which is formed on the surface of the pericardium produces a marked alteration there. Instead of a smooth glistening surface, allowing the visceral to glide gently and easily over the parietal portion of the membrane, there is a coating of lymph which is so soft that its surface gets roughened by the rubbing to which it is subjected, and becomes more or less ragged and shaggy in appearance. The rubbing

against each other of the thus roughened surfaces of the pericardium produces the "to and fro" friction sound characteristic of the disease. This sound is generally double; but may be single, and then is usually short, and may be with difficulty distinguished from an endocardial murmur. It is generally heard first near the base of the heart; but it may be distinct over the whole organ. It is superficial in character, like a pleuritic rub; but easily distinguished from that by its situation, and by its being independent of the respiratory movements. There is no increase of cardiac dulness. This is the stage at which any subjective symptoms which may exist are usually felt.

The morbid process may go no further than this. The inflammation may decline; the lymph may be reabsorbed; and the pericardium be restored to its natural state. Or the two roughened surfaces may adhere together to a greater or less extent.

In acute cases there is generally a third stage, characterised by the effusion of serum into the sac of the pericardium. A certain amount of fluid is thrown out during the second stage at the same time as the lymph. The quantity may be so small that it gives no physical evidence of its existence, and is quickly absorbed when the inflammation subsides. The presence of a larger quantity gives very decided evidence of its existence. It separates the visceral from the parietal layer of the pericardium. Rubbing of these surfaces against each other thus becomes impossible,

friction ceases to be heard, and any pain which there may have been disappears. The area of cardiac dulness is increased. If the sac of the pericardium be quite full, the region of dulness has the triangular shape of that sac—with the apex above and the base below. The dulness extends to the left of, and beyond, the apex point. The heart's impulse is not felt as in hypertrophy of the organ. The sounds are distant and indistinct. The pulse is quick and feeble—maybe irregular. There is increased frequency of respiration; and the patient may be in considerable distress.

Under proper treatment, and in the absence of other complications, the fluid is generally absorbed. As it diminishes in quantity, the region of cardiac dulness also decreases. The two layers of the still roughened pericardium once more come into contact; and friction may be again heard for a day or two. Here, as in the case in which recovery takes place at the end of the second stage, the friction gradually disappears, and ultimately everything seems to return to its natural state—recovery being apparently perfect. It is doubtful, however, if the pericardium ever quite regains its natural condition. It may possibly do so in some cases; but in most instances more or less extensive adhesions are formed between its two layers. Where the inflammation has been severe, such adhesions are formed over the whole surface of the heart, and the sac of the pericardium is obliterated.

Such obliteration has been regarded by some as a

source of much embarrassment to the heart's action, and a cause of hypertrophy and dilatation of that organ. By others it has been said to produce some degree of atrophy of the heart. While a third set of observers maintain that an adherent pericardium gives rise to no symptoms during life, and to no morbid change in the muscular substance of the heart.

It is probable that the age and mode of life of the patient have much to do with the variety of the results noted by different observers. It is in young and excitable persons, and in those whose habits or tastes lead them to take much exercise, that obliteration of the pericardial sac causes inconvenience. The function of the pericardium is to provide for the free and active movements of special occasions and unusual efforts. If such occasions do not arise, and such efforts are not made, the obliteration of its sac causes no embarrassment, and no change in the heart. The ordinary work of that organ can be quite well done without the pericardium; and so long as this work is not unduly increased, and extraordinary efforts are not required, no harm results from the obliteration of its sac. It is for the free movements of special occasions that it is required. "The free motion of the heart within the pericardium is required in health, not so much to meet the necessities of the circulation in its tranquil and ordinary condition, as to provide for the contingency of excited action, and to give abundant scope for the smooth and painless motion

of the heart under those circumstances in which the habitual equilibrium of the circulation is disturbed."¹

It is doubtful if a severe attack of pericarditis, resulting in obliteration of the sac of the pericardium, ever occurs without the muscular structure of the heart participating more or less in the morbid process. The evidence of its being affected would be lost in the more prominent signs of the pericarditis. Such myocarditis might lead to subsequent change in the heart—a change which would not unnaturally be attributed in the *post-mortem* room to the obliteration of the pericardium.

Occasionally the fluid effused into the pericardial sac becomes purulent; but such an occurrence is much more rare than in inflammation of the pleura.

There is one fact in the history of rheumatic pericarditis which has a most important bearing on the pathogenesis of the disease. This fact is, that the disease almost always commences in the visceral layer of the pericardium, and at the base of the heart.

The evidence of this is as follows:—

(1) In slight and circumscribed attacks, the inflammatory change is, as a rule, confined to this portion. Affecting only the visceral layer, and only a small part of it, there may be no physical signs or symptoms by which its existence may be diagnosed. But we know that such slight attacks do occur; for in the *post-*

¹ "On the Favourable Terminations of Pericarditis," by W.T. Gairluer, M.D., *Edinburgh Monthly Journal of Medical Science*, 1851.

mortem room it is not uncommon to find some thickening and opacity, the result of inflammation of this part of the pericardium, without any other evidence of the disease having existed.

(2) In cases in which the disease spreads over the body of the heart, and affects both layers of the pericardium, the friction sound is generally heard first near the base.

(3) In cases in which death takes place in the early stage of the disease, it is found that while that part of the membrane which is situate over the body and apex of the heart is merely hyperæmic,—is still in the first stage of inflammation,—that which surrounds the origin of the great vessels at the base has reached the second stage, and is covered with shreds of lymph. “In ordinary acute pericarditis the earliest stage is seen as a minute injection of its vessels, causing a blush of redness, which close observation resolves into a beautiful red network. This injection is almost a certain proof of pericarditis, but when you see it you should look at the base of the heart, about the great vessels, where you will always find some shreds of inflammatory lymph.”¹

Is there any possible explanation of these facts—any reason why the rheumatic poison should act primarily and chiefly on this part of the pericardium? There is no structural peculiarity to account for it. It cannot be due to greater functional activity; for

¹ Wilks and Moxon, *op. cit.*, p. 98.

movement is freer at the apex than at the base. The only peculiarity of that portion of the pericardium which seems specially liable to rheumatic inflammation is that it is situate over, and in near contact with, the fibrous textures of the heart—in near contact, that is, with that particular portion of the cardiac structures which is specially liable to suffer from the action of the rheumatic poison. The inference is inevitable, that inflammation of the pericardium may be due, not to the direct action of the rheumatic poison on that membrane, but to the extension to it of an inflammatory process originating in the subjacent fibrous textures. We have already seen that inflammation of the inner lining membrane of the heart is limited to that part of it which is in direct relation with the fibrous rings and valves, and is secondary to inflammatory change in these structures. There is not a little evidence to show that in many cases inflammation of its outer investing membrane has primarily a like limitation and a similar pathology.

When considering the pathogenesis of the joint troubles of acute rheumatism, we saw good reason to think that inflammation of the synovial membrane was secondary to inflammation of the ligaments and tendons. There is equally good reason to believe that it may, in like manner, extend to the pericardium from the fibrous textures of the heart; and that to such extension rather than to the direct action of the rheumatic poison on that membrane many cases of pericarditis are due.

CHAPTER XIV

MYOCARDITIS

WHEN considering the question of the action of the rheumatic poison on the various structures involved in acute rheumatism, we saw that the voluntary muscles were directly affected by it, and that the excess of lactic acid characteristic of the disease was a consequence of increased muscle metabolism.

If the voluntary muscles are thus affected, there is no reason why the cardiac muscles should escape, for they are similar in structure and function. Indeed, in their case there is distinct and direct evidence that they do thus sometimes suffer during the course of rheumatic fever, for many cases have been recorded in which the cardiac walls have been found, after death, to be the seat of inflammatory softening, induration, or even suppuration. With this evidence of myocarditis there has usually been associated the usual *post-mortem* signs of endocarditis, of pericarditis, or of both. The existence of this association, the difficulty of diagnosing myocarditis during life, and the rarity of *post-mortem* evidence of its existence

except in combination with inflammation of the membranes, has led to the inference that inflammation of the muscular substance is secondary to that of the membranes, and results from the direct extension to it of an already existing inflammation of one or both of these.

Myocarditis occurring independently of endo-pericarditis is described by Walshe¹ as "an affection, to say the least, of extreme rarity."

Peacock² says that myocarditis "is rather interesting in a pathological point of view than practically important. It probably always occurs in connection with one or both the other forms of disease," *i.e.* endocarditis or pericarditis.

"Inflammation of the heart substance is frequently set up in the layers contiguous to an inflamed endocardium or pericardium."³

"Inflammation of the muscular substance of the heart rarely occurs except in connection with peri- or endo-carditis. In pericarditis a greater or less thickness of the muscular walls in contact with the inflamed serous membrane is often distinctly implicated; and there is no doubt that their inner aspect may be similarly involved during the course of an attack of endocarditis."⁴

But when we come to examine the grounds on

¹ *Diseases of the Heart*, 4th ed., p. 263, 1873.

² *St. Thomas's Hospital Reports*, 1875, p. 12.

³ *The Theory and Practice of Medicine*, p. 39, by F. F. Roberts, M.D., F.R.C.P., 3rd ed., 1877.

⁴ *The Theory and Practice of Medicine*, p. 516, by J. S. Bristowe, M.D., F.R.C.P., 1876.

which this opinion is based, we find that they are scarcely adequate to its support, and that especially the view that myocarditis is secondary to, and dependent on, prior inflammation of the endocardium is one which can hardly be maintained. The lining membrane of the heart is a non-vascular structure, in which inflammation cannot, and, as a matter of fact, does not spread. The morbid change which takes place in it during the course of acute rheumatism is secondary to change in the subjacent fibrous tissue, and is limited entirely to that part of the membrane which is reflected over the fibrous valves. It never extends to the much more extensive portion which lines, and is in contact with, the muscular substance, and from which alone it could extend to that substance. Limited as the morbid process thus is, showing no tendency to spread, and never affecting the part of the membrane which is in contact with the muscular walls, it is simply impossible that inflammation should extend from the endocardium to the muscular substance of the heart. Endocarditis and myocarditis may coexist, but the latter cannot be secondary to the former.

It is different with the pericardium; it is a very vascular membrane in which inflammation readily spreads; the whole membrane may suffer, and its inflamed part be in direct contact with the muscular walls. It is quite possible, therefore, that inflammation may extend from it to them; it is equally

possible that the process may occasionally be reversed, and that inflammation may extend from the muscular walls to the pericardium. But more probable than either is it that when pericarditis and myocarditis coexist each occurs independently of the other—both being part of a general carditis.

The part of the heart which most suffers in rheumatic fever is the fibrous structure of the rings and valves. We have seen that inflammation of the endocardium is always secondary to a prior inflammation of the fibrous structure of a valve; and that there is good reason to believe that in many cases of pericarditis the inflammation spreads to that membrane from the fibrous structures at the base of the heart. If inflammation spreads from these structures to the endocardium and the pericardium, there is no reason why it should not equally extend to the muscular substance. There is every facility for its doing so, for the muscles of the heart are attached to the fibrous rings: and it is probable that many cases of partial myocarditis, in which the inflammation is limited to the base of the heart, are so produced.

Rheumatic myocarditis, like rheumatic endocarditis, is almost entirely confined to the left ventricle, and for the same reason. It may be partial or general, involving a part, or implicating the whole structure of the muscular wall. The partial is the more common. Its situation is the base of the ventricle. It is probably due in most cases to an extension to the muscles

of a prior inflammation of the fibrous structures. As there is usually a similar extension of that process to the endocardial lining, any symptoms to which the myocarditis might give rise are apt to be attributed to the more obvious endocarditis. The evidence of its occurrence is found in the *post-mortem* room in the form of circumscribed patches of induration of the muscular wall of the ventricle; chiefly at the base, and generally in company with thickening and induration of the fibrous rings and valves.

General rheumatic inflammation of the walls of the left ventricle, like other local inflammations, occurs in varying degrees of severity. When very acute, it may give rise to such destructive change in the ventricular walls that recovery is impossible. In a less severe form, it causes simply softening of the ventricular walls—a condition which may be perfectly recovered from, or may result in more or less induration of the muscular substance; but which may also be a cause of sudden death.

Myocarditis is a formidable disease, apt to be fatal, and apt to be overlooked. It is apt to be fatal, because of the importance of the tissue inflamed; it is apt to be overlooked, because of the obscure and even misleading character of some of its most common and prominent symptoms.

Corvisart¹ divided cases of myocarditis into two

¹. *Essai sur les Maladies et les Lésions Organiques du Cœur et des Gros Vaisseaux*. Paris, 1818. 3me ed.

classes,—the *distinct*, and the *latent*,—those in which the symptoms clearly indicate the nature of the disease, and those in which symptoms directly referable to the heart scarcely exist.

Acute pain in the epigastrium, or præcordial anguish, a sense of oppression and anxiety, embarrassed respiration, the evidence of defective aeration of the blood without any pulmonary lesion to account for it,—such are the symptoms which may present themselves in distinct cases of myocarditis. Seldom, if ever, do they all exist at the same time. Now one, now another predominates. The most common are præcordial uneasiness, and evidence of defective aeration of the blood. With these there are associated symptoms of disturbance of the sensorium.

Myocarditis may be accompanied by inflammation of the endocardium or pericardium, or both. It is then part of a general carditis. The physical signs of the membranous inflammation are so obvious, that all the symptoms are apt to be ascribed to it. It is probable that the less obvious myocarditis plays a not unimportant part in the production of many of them; though how much of the patient's disturbance is due to the membranous, and how much to the muscular inflammation, it is impossible to say. It is a matter of course that when both the walls of the ventricle and the membranes are inflamed, there is likely to be greater disturbance and irregularity of the heart's action, and a greater tendency to death, than when

the membranes only are involved. But it is impossible to diagnose the extent of the myocarditis as we do that of the endo-pericarditis. All that we can say is that if, in the course of a case of rheumatic inflammation of the membranes, we find either a marked degree of cerebral disturbance, without hyperpyrexia, or evidence of defective blood purification, without any pulmonary lesion, or any serious amount of pericardial effusion, we may feel sure that the muscular substance of the heart is seriously involved in the mischief.

The physical signs of the membranous inflammation so predominate over any change in the cardiac sounds to which the myocarditis might give rise, that we can better diagnose the existence, and gauge the extent of this latter, by careful observation of the general symptoms, than by a physical examination of the heart.

There are cases of acute myocarditis, as of acute pericarditis—Corvisart's latent cases—which run their whole course to a fatal termination without any symptom directly referable to the heart; the only symptoms being those of cerebral disturbance. An admirable illustration of this is found in a case recorded by Mr. Stanley in the seventh volume of the *Medico-Chirurgical Transactions*, 1816. So far as I know, it is the earliest recorded case of the kind.

“A boy, aged twelve years, although of a delicate frame; had enjoyed generally a good state of health. On Saturday, the 20th of April, he was

apparently quite well, having been on that day on a visit to one of his relations by whom this remark was made. On the next morning he was brought to the Infirmary, discovering at that time the usual symptoms of fever, namely, great bodily heat, a quick pulse, the tongue white and much furred. On the next day (Monday) his fever was much increased, but the only pain of which he complained was in the left thigh and knee, which ceased before night; in the afternoon he became delirious with much watchfulness. On Tuesday the delirium was very considerable, but without any comatose tendency; the pupil of the eye much dilated, but not insensible to light. He complained but little of pain, but when closely pressed upon the subject, he pointed to his forehead. Early in the afternoon of that day he had a convulsive fit which soon went off. In the evening all his symptoms became aggravated, and he passed the night almost without sleep. On the following morning he appeared much sunk; his breathing for the first time became difficult. He was then sufficiently sensible to answer any question put to him, but soon afterwards he became insensible, and gradually declined till about two in the afternoon, when he expired."

Those who saw this boy thought that his symptoms were of cerebral origin, and "that there was effusion within the head."

The idea of there being anything the matter with the heart did not suggest itself to his attendants;

and "at no period of his illness did he complain of pain in any part of the thorax, nor was there any irregularity, either in the action of the heart or pulsation of the arteries."

"It having been considered from the general character of the symptoms that the cause of death was to be sought in the head, this was the part first inspected; but after an attentive examination of the brain, nothing further could be remarked than that the vessels were generally turgid; not more so, however, than is frequently seen when death has taken place under circumstances that lead to no suspicion of affection of the head." The abdomen was healthy. So were the lungs. "On opening the pericardium it was found to contain between four and five ounces of turbid serous fluid, with flakes of coagulable lymph floating in it. The internal surface of the membrane, both where it constituted the exterior bag, and the reflected layer upon the heart, was covered in various situations with a thin layer of lymph exhibiting a reticulated appearance. The size of the heart was natural in relation to the age of the patient. Upon cutting through its parietes the fibres were exceedingly dark coloured, almost of a black appearance. This evidently depended on the nutrient vessels being loaded with venous blood. The fibres were also very soft and loose in their texture, being easily separable, and with facility compressed between the fingers. Upon looking closely to the cut surface exposed in the section of either

ventricle, numerous small collections of dark-coloured pus were visible in distinct situations among the muscular fasciculi. Some of these depositions were situated deeply, near to the cavity of the ventricle, while others were more superficial, and had elevated the reflected pericardium from the heart. The muscular fibres of the auricles were also softened in their texture, and loaded with blood, but without any collections of pus between them. All the cavities of the heart were loaded with coagulated blood. The internal lining, valves, and every other part of the organ exhibited nothing worthy of remark, except the state of general turgescence in the capillary vessels, which had also extended to the lower part of the trachea, bronchi, etc."

This case serves well to show that we may have inflammation of the muscles of the heart, sufficiently severe to give rise to suppuration, and to prove fatal in a few days, without a single symptom to call special attention to that organ. It also indicates, though in an unusually marked manner, the character of the general symptoms on which we have to rely for a diagnosis. It may usefully be read along with Andral's case of pericarditis quoted at p. 144.

There are absolutely no physical signs by which the existence of myocarditis can be determined. There may be indications of cardiac weakness, the impulse may be diffuse, or the apex beat imperceptible, and the first sound muffled or indistinct, or reduplicated, but this is not enough for a diagnosis. It is to the

general symptoms that we have to trust, and these are essentially the indications of nervous disturbance—mainly delirium.

Delirium in acute rheumatism is always a symptom of serious import. It is so because of the serious nature of the complications of which it is symptomatic. It occurs in hyperpyrexia, in myocarditis, in pericarditis, and in pneumonia arising in the course of acute rheumatism.

In hyperpyrexia there is the thermometer to guide and give precision to the diagnosis. In pericarditis and in pneumonia equal precision is obtained from a physical examination of the heart and lung. But in myocarditis we have no such aid; we have to trust to the general symptoms only. It may be stated generally that delirium arising in a case of acute rheumatism, complicated neither with pericarditis nor pneumonia, and in which the temperature is not over 105° , is symptomatic of myocarditis. The delirium may be acute, generally it is low and muttering. With it there are sometimes noted muscular tremors which may give to the patient somewhat the appearance of one suffering from delirium tremens.

A man, aged twenty-five, of irregular rather than of dissipated habits, had an ordinary attack of acute rheumatism, with the characteristic joint affection and acid sweats of the disease. The temperature ranged from 102° to 103° Fahr. He was treated with salicylate of soda. His joint pains decreased,

but his general condition did not improve. On the eighth day of his illness, on which I first saw him, he was very prostrate; there was some tenderness on pressure over both wrists, the left knee and right shoulder, but the joint indications were not marked; there was very little swelling, and pain was not complained of, except on pressure or movement; temperature was 103.8° , tongue furred, pulse 120, feeble; the heart's sounds were indistinct, and the systole feeble, but no bruit could be detected; the area of cardiac dulness was normal. The patient was prostrate, and sunk in bed; though he understood what was said to him, he took no notice of what went on around him; the tongue was dirty, and dry in the centre; there was muttering and wandering, most marked during the night. The patient was freely stimulated and carefully nourished, but he gradually sank and died.

On *post-mortem* examination all the organs were healthy except the heart. The pericardium contained about an ounce of dark-coloured serous fluid; around the roots of the great vessels at the base there was a slight deposit of recently effused lymph, but the general surface of the pericardium was smooth and glistening. The muscular substance of the heart was dark in colour, and had the appearance of being gorged with blood; it was soft in consistence, and could be broken down by pressure between the finger and thumb; under the microscope the individual

fibres were seen to have lost much of their normal striated appearance, and to be somewhat granular in aspect. There was slight roughening of the auricular surface of the mitral valve; but no other appearance of endocardial mischief.

The general aspect of the patient in this case was not unlike that noted in some cases of hyperpyrexia, and had there been a high enough temperature, one would not have hesitated to call it so. *Post-mortem* examination verified the accuracy of the diagnosis formed during life; that the alarming symptoms were due to inflammation of the muscular substance of the heart.

A man, aged forty, had an ordinary attack of acute rheumatism, with inflamed and swollen joints, acid sweats, and a temperature varying from 101° to 102.4° . He was treated by alkalies and salicylate of soda. Though his pains were less, and the temperature fell a little, he did not make satisfactory progress. On the seventh day of his illness (that on which I first saw him) the temperature was 101° , the pulse was 108° , feeble and compressible; the skin was moist, the perspiration acid; the tongue moist and furred; there was pain and swelling in both ankles, right knee, and both wrists. Patient was depressed and sunk in bed; the hands were tremulous; he wandered at night, and occasionally during the day; the bowels were moved by medicine. The area of cardiac dulness was normal; there was no bruit, but the sounds

were indistinct, and the apex beat could not be felt. The diagnosis was myocarditis—inflammation of the muscular substance of the heart. He was ordered to have, every two hours, four ounces of milk or strong beef-tea, with half an ounce of brandy. All movement was forbidden; as medicine, fifteen grains of salicin were given every two hours. He gradually improved, the muttering delirium ceased, the tongue cleaned, he was less sunk in bed, and got some hours of quiet sleep, and the joint pains disappeared. On the nineteenth day there was heard for the first time a distinct pericardial to-and-fro rub, audible only at the base of the heart. This persisted for two days, and then disappeared. Cardiac dulness remained normal, and there was no evidence of fluid effusion into the sac of the pericardium. The patient picked up slowly, but ultimately got well. A year after his illness I examined the heart and found nothing amiss in it.

By various observers attention has been directed to the occasional occurrence of sudden death in acute rheumatism. It is probable that the explanation of this result is to be found in inflammatory softening of the ventricular walls. It certainly was so in the following case.

A girl, aged twenty, who had previously enjoyed good health, suffered from an attack of acute rheumatism in March 1872. The attack was an ordinary one of medium severity, presenting no unusual feature,

but complicated by a slight attack of endocarditis, which gave rise to no subjective symptom; and the only sign of whose existence was a soft and short systolic blow at the apex. She was treated with acetate of potass, ten grains every three hours. (The case occurred before the days of the salicyl treatment.)

The endocardial blow persisted, but the rheumatic symptoms had diminished in severity by the end of the second week. On the seventeenth day of her illness she got up of her own accord. Her sister, who was in the room, stated that her feet had scarcely touched the floor, when she fell back on her bed, and lay there motionless. She never moved, or gave any sign of life. I saw her twenty minutes later, quite dead. A few minutes before making the effort, she expressed herself as feeling very well, and free from pain.

On *post-mortem* examination, the mitral valve was found to be somewhat thickened, and on its auricular surface was a line of lymph deposit. The heart's substance, especially that of the left ventricular walls, was rather dark in colour, and softer than natural. On firm pressure, it broke down under the finger. On microscopic examination, the normal striæ were wanting in distinctness; and here and there the fibres had a granular aspect. There was a little effusion into the pericardium. There was no ulceration of the endocardial surface; no appearance of embolism; nothing to explain the fatal result, except the altered

condition of the ventricular walls. The cranial and abdominal contents were normal.

A man, aged thirty-three, who had had several attacks of acute or subacute rheumatism, had what he regarded as one of his ordinary attacks which he tried to manage for himself with his usual mixture of salicylate of soda, without going to bed. Getting worse I was asked to see him. I could not go, and asked a *confrère* to do so. He reported to me that the man had subacute rheumatism, with a temperature of 101°; but that he had symptoms of delirium tremens as well, though he did not think he had been taking much stimulant. I knew that he was a man of steady habits, and thought it likely that the tremors and delirium were symptomatic of myocarditis, and arranged to see him the following day; but, in the meantime, while undressing to get into bed he suddenly died. No *post-mortem* could be got.

I had seen the man some months before and examined the heart, which was then quite healthy. There was, therefore, no old-standing heart trouble to account for the death. But there were during life the nervous symptoms which accompany myocarditis; and there can be little doubt that this was the cause of death. Indeed, symptoms resembling those of delirium tremens coming on in the course of acute or subacute rheumatism in a man of steady habits, and in whom there is no great rise of temperature, are almost certainly due to myocarditis.

The *post-mortem* appearances presented in cases of myocarditis, like the symptoms during life, are not very obvious, though quite distinct when carefully looked for. They consist chiefly in loss of consistence in the ventricular walls (for the disease is generally limited to the left ventricle). The muscular substance is darker in colour than natural; it has lost its naturally firm consistence, and may be so soft as to break down on being pressed between the finger and thumb. On microscopic examination the individual fibres are seen to have lost more or less completely their normal striated appearance, and to be granular in aspect. The inflammation may even go on to supuration, as in Mr. Stanley's case already quoted. But that is very rare.

The treatment of myocarditis essentially consists in keeping the heart agoing till the inflammation is over and the weakened muscular fibres regain their normal condition. Absolute quiet and rest must be insisted on. Good nourishment and a liberal allowance of stimulants are important. Opium may be of service by relieving pain, allaying restlessness, and storing nerve power. At the same time the rheumatism to which the myocarditis is attributable is not to be lost sight of. The undoubted tendency of the salicylates to disturb the nerve centres and enfeeble the cardiac action in a certain number of cases is a reason why they should not be given; but salicin, which has no such untoward effect, should be given in sufficient

dose to counteract the rheumatic process—fifteen to twenty grains every two or three hours.

When the acute symptoms are subdued and the immediate danger of heart failure is over, a distinctly tonic treatment is called for.

The points to be insisted on are :—

(1) That myocarditis may occur in acute rheumatism independently of inflammation of the membranes of the heart.

(2) That it gives rise to no physical signs by which its occurrence can be diagnosed.

(3) That the symptoms by which it is to be recognised are those of disturbance of the nervous system occurring in acute or subacute rheumatism without the high temperature of hyperpyrexia, and without other apparent cause.

CHAPTER XV

THE TREATMENT OF RHEUMATISM

IF the pathology of rheumatism has been unsatisfactory, its treatment has been not less so. There is probably no disease in which so many different modes of treatment have been had recourse to. There is none in which medicinal treatment has, until within recent times, more completely failed to shorten the duration of the malady. The special mode of treatment in vogue at a given time has generally depended on the views held regarding the nature and mode of production of the disease. During the last century, and the first half of this, rheumatism was regarded as a "phlegmasia"—as an inflammation dependent, like other inflammatory affections, on exposure to cold, and differing from them only in the nature of the textures involved. The treatment of inflammation was, at that time, essentially antiphlogistic, and consisted in the adoption of various means of depletion. The chief of these was bleeding. Sydenham wrote in 1666 that "the cure of rheumatism is to be sought by blood-letting." His rule was to take ten

ounces of blood as soon as he saw the patient, to repeat the operation the following day, to do it again in a day or two, and, for the fourth and generally the last time, three or four days later. But he was not satisfied with the results of this practice; for in 1679, ten years before his death, he says in a letter to Dr. Brady, "I, like yourself, have lamented that rheumatism cannot be cured without great and repeated losses of blood. This weakens the patient at the time; and if he have been previously weak, makes him more liable to other diseases for some years. . . . Reflecting upon this, I judged it likely that diet, simple, cool, and nutritious, might do the work of repeated bleedings, and saving the discomforts arising therefrom. Hence I gave my patients whey instead of bleeding them." He gives the particulars of a case treated dietetically, in which the patient "recovered his full strength, escaping all such discomforts as ten years before a similar attack, which I treated by bleeding, had entailed upon him."

Cullen, though he regarded blood-letting as "the chief remedy of acute rheumatism," and taught that "large and repeated bleedings during the first few days of the disease seem to be necessary," was careful to add that "to this some bounds are to be set; for very profuse bleedings occasion a slow recovery, and if not absolutely effectual, are ready to produce a chronic rheumatism."

Though the indiscriminate use of the lancet was

condemned by other able observers, such as Heberden, Fowler, Latham, etc., bleeding continued, till well on in this century, to be the sheet-anchor in the treatment of acute rheumatism.

“In undertaking the treatment of acute or sub-acute rheumatism, whether we view the inflammatory state of the aponeurotic membranes as primary and idiopathic, or secondary and symptomatic, it is necessary in the first instance to adopt the antiphlogistic method of treatment, and to carry it on with some degree of energy, and to a considerable extent.

“The different branches of the antiphlogistic regimen requisite in the treatment of rheumatism are blood-letting, general and local, the occasional employment of cathartics, the occasional employment of emetics, especially tartar emetic, the use of diaphoretics, and the use of revellents. . . .

“*First.* General blood-letting, in order to be beneficial, ought to be performed early in the disease, and carried to a considerable extent. . . . It should be carried at first to twenty or twenty-five or thirty ounces at once if possible; and within twenty-four hours to as much more.

“*Secondly.* The influence of general blood-letting must be aided by the conjoined operation of various adjuvants. Full vomiting produced by ipecacuanha and antimony is in the majority of cases requisite; and complete evacuation of the bowels by eccoprotics and even cathartics is quite indispensable.

“*Thirdly.* It is of the utmost importance, in attempting the thorough removal of rheumatic pains, to conjoin with blood-letting, or after its use, the administration of full doses of tartrate of antimony.

“*Fourthly.* It is of great moment, if the bowels have been previously well opened, to exhibit, after the first blood-letting, an opiate of forty or fifty minims of the solution of muriate of morphia; or if the bowels have not been freely moved, to effect this indication, and take a second blood-letting, and after this to administer the opiate, which may be either given alone or conjoined with antimony.”¹ So wrote Dr. Craigie in 1840. In that year appeared also Bouillaud’s *Traité Clinique du Rhumatisme Articulaire*, in which the treatment by bleeding *coup sur coup* was advocated with characteristic ability and energy.

To Bouillaud, indeed, belongs the credit of having systematised this mode of treatment. The full extent of his credit in this respect is not generally recognised. Previous to his time the practice of phlebotomy was wanting in method. To take so many ounces of blood, and to repeat the operation in one, two, or more days, was all the recommendation. Bouillaud insisted that there should not be too long an interval between the different bleedings—that the second should be had recourse to before the effects of the first had fully passed off, and the third before the benefit of the

¹ *Elements of the Practice of Physic*, by David Craigie, M.D., F.R.S.E., vol. ii., 1840.

second was lost. That is what he meant by his recommendation to bleed *coup sur coup*. It was the frequent repetition of the operation, rather than the quantity of blood taken, which formed the characteristic feature of his mode of treatment. If the pathological views which then prevailed were correct, and if bleeding were the important therapeutic agent which it was believed to be, there can be no doubt that Bouillaud's idea was therapeutically sound. No single dose of any remedy could stop a disease like acute rheumatism. It would have to be repeated from time to time ; and to get its full beneficial effects the second dose would have to be given before the first had quite ceased to act. Bouillaud's merit consists in having applied this sound therapeutic rule to the practice of phlebotomy.

About the middle of this century the practice of phlebotomy, and the pathological views on which it was founded, were vigorously assailed. Facts tended to show that patients recovered more quickly and satisfactorily when they were not bled than when they were. This was noted in acute rheumatism, as in other acute diseases. The rapid accumulation of such facts produced a marked reaction against the old mode of treatment ; and within twenty years of the time that Bouillaud's book appeared, the practice of bleeding in acute rheumatism was all but abandoned.

Other remedies besides bleeding were used to allay the inflammation.

Purgatives were at one time a good deal used. Those most in vogue were the saline, chiefly the sulphates of magnesia and soda. Calomel was also thus employed, especially by Latham, and with results which gave satisfaction.

Diaphoretics, especially ipecacuanha and antimony in combination with opium, have been at all times much used. Dover's powder has enjoyed a specially high reputation. Referring to it, Cullen says, "Notwithstanding what I said in favour of venesection, I must own that I never saw a cure very quickly expedited by venesection alone, in the cure of any violent case of the disease; for the disease is liable to linger, and continue for a long time, and to pass into a chronic state. The Dover's powder gives us an opportunity of more effectually and more safely curing the disease than by bleeding alone."

Opium alone, except as a diaphoretic, was condemned by Cullen; but has had much said in its favour in more recent times by Corrigan, Trousseau, and others.

Cinchona, and its alkaloid quinine, have at different times had their claims to favourable consideration pressed. Morton was the first to use cinchona in acute rheumatism. Cullen gave the great weight of his authority against it. He regarded its employment as "absolutely improper and manifestly hurtful," except in cases in which the acute stage had been subdued by bleeding and other measures, and

in which the ailment threatened to become periodic. Haygarth,¹ who first used it on the recommendation of Dr. Fothergill, brought forward much testimony in its favour. George Fordyce² used it early and freely. Its alkaloid quinine was at one time freely used, especially in France. A suspicion that it gave rise to cerebral symptoms and dangers, prevented many from trying it, notwithstanding the strong recommendations of Briquet, Monneret, and others. Garrod³ tried to revive this treatment in a modified form. He gave the quinine along with carbonate of potass—five grains of the former and thirty grains of the latter, every four hours “until the joint affection and febrile disturbance have completely abated.” The benefits which he claims for this plan are its greater efficacy, a diminished tendency to relapse, and a more satisfactory convalescence.

Colchicum has been much used in the treatment of rheumatism; but there is no valid evidence of its exercising any beneficial action. Garrod, who regards its power to subdue gouty inflammation as beyond doubt, says that “it possesses no influence in checking the progress of rheumatic fever.” To give relief to the pain of rheumatism, it requires to be given in quantity large enough to cause depression of the heart’s action; and that is a condition which

¹ *Clinical History of Diseases*, Part I., 1805.

² *Elements of the Practice of Physic*, 1791.

³ Reynold’s *System of Medicine*, article “Rheumatism,” vol. i., 1866.

cannot safely be induced in the course of an ailment which tends specially to affect the heart.

Guaiacum has long enjoyed considerable reputation as a remedy in rheumatism. Originally introduced by Dr. Dawson, it found its chief advocate in Fowler, who regarded it as useful in all stages of the disease. It is nowadays prescribed chiefly in the chronic form.

Nitrate of potass was at one time a good deal used as a diuretic and refrigerant in febrile ailments Brocklesby recommended it in acute rheumatism. He gave as much as two drachms dissolved in some diluent three, four, or five times a day. Given thus, there was got both a diaphoretic and diuretic action. This treatment was revived by Dr. Basham, who not only gave the nitre internally, but also applied it locally to the inflamed joints. The results of this treatment seem to have been as good as those of any other.

Other remedies, aconite, veratrine, digitalis, *actæa racemosa*, etc., have enjoyed a passing reputation, and had their claims advocated by different observers. But not one of them has stood the tests of time and investigation.

About the time that bleeding went out of fashion, new views began to be entertained regarding the pathology of rheumatism. This was all but inevitable. If bleeding was wrong, the pathological view on

which that treatment was founded was also likely to be erroneous. If to take blood not only did no good, but even did positive harm, then were there grave reasons for questioning the soundness of what was generally believed regarding the nature of rheumatism. Doubts were started, investigation was stimulated, the symptoms of the malady were subjected to fresh scrutiny, the opinions of the older writers were regarded with a healthy scepticism, and by and by new views began to be ventilated. The question began to be discussed whether rheumatic inflammation was not altogether peculiar, and due to some special poison circulating in the blood, rather than to the operation of cold.

The acid condition of the secretions attracted early and prominent attention, and was regarded as a possible cause of the rheumatism. Prout made the definite suggestion that lactic acid was the rheumatic poison. Ably advocated by Todd, Fuller, and others, this view was soon generally accepted. Altered views of causation led to altered treatment. If lactic acid were the rheumatic poison, it was plain that the proper treatment was to promote its elimination, and to counteract its effects.

"It is probable," says Todd, "that the *materies morbi* in rheumatic fever is lactic acid or some analogous agent. We know that the natural emunctory of this is the skin. Many chemists maintain that it will also escape by the kidneys; and if it

ever does so, perhaps this is more likely during rheumatic fever than at any other time.

“Again, since vitiated digestion is apt to produce it in undue quantity, and it, therefore, is formed abundantly in the stomach, there is every reason to think a certain proportion of it may be carried off through the alimentary canal. The indications are, then, to promote the action of the skin, the kidneys, and the bowels; to use antacid remedies; and to give large quantities of fluid for the free dilution of the *materies morbi*, and to supply the waste caused by the drainage from diaphoresis and diuresis.”¹

The acid theory naturally led to alkaline treatment; and that continued till very recently to be *the* treatment for rheumatism. “If the *materies morbi* be indeed an acid or an acidulous compound—if it be lactic acid, for instance, as there are cogent reasons for believing it to be,—then will its neutralisation be effected, its irritative property probably diminished, and its elimination promoted, by a free exhibition of alkalies and neutral salts.”²

The alkaline salts chiefly used have been the bicarbonate and acetate of potass, given in the dose of fifteen to thirty grains every three or four hours. The evidence adduced by Fuller, Garrod, Basham, and others in support of this treatment, is sufficient

¹ Todd's *Clinical Lectures*, p. 69.

² Fuller *On Rheumatism*, p. 77.

to demonstrate its superiority over any which preceded it. But the sanguine anticipations of its earlier advocates have not been realised; for it has been found in practice that alkalies may be given so as to render the urine alkaline, without diminishing the joint pain or allaying the fever.

As time advanced, and facts accumulated, it became evident that the alkaline treatment did not materially shorten the natural duration of acute rheumatism, or decidedly diminish the tendency to heart complications—the two advantages which had been specially claimed for it.

We have already seen that the theory on which that treatment is based is untenable, and that lactic acid is not the rheumatic poison, but only one of the results of the rheumatic process.

The theory on which the alkaline treatment was founded being erroneous, we are not surprised to find that treatment fail to produce the good results which its early advocates anticipated.

Impressed with a sense of the failure of this mode of treatment, physicians looked about for something better. Owen Rees used lemon-juice, and got from it results which were at least as good as those which followed the administration of alkalies. Some gave up all medicinal treatment, and simply kept the patient warm in bed, gave him a light simple diet, and administered some *placebo*. Dr. Flint¹ published

¹ *American Journal of the Medical Sciences*, July 1863.

in 1863 an account of thirteen cases treated on this plan with good results. Two years later an equally good report was given by Dr. Sutton,¹ of forty-one cases treated in Guy's Hospital, and which got medicinally only mint water. This expectant plan of treatment was adopted by many, with results as satisfactory as those got from more active measures.

"I am quite certain," says Sir Alfred Garrod, "that many cases, even of severe rheumatic fever, get rapidly well without the administration of drugs; and on simply coloured or camphor water the improvement is often so quick and satisfactory that, had not the nature of the treatment been known, great virtue would surely have been ascribed to it."

This expectant plan of treatment is really that which was recommended and practised by Sydenham in the later part of his career. To treat a patient by mint water, is practically the same as treating him by whey, which Sydenham did two hundred years ago. It is curious to find the physicians of the nineteenth century going back to the same plan of treatment which was recommended by the father of English medicine in the seventeenth.

Sir Russell Reynolds, dissatisfied with the alkaline treatment, tried in acute rheumatism a remedy which had proved serviceable in some forms of spreading inflammation—the tincture of muriate of iron. His results were as good as those got by any other treatment.

¹ *Guy's Hospital Reports*, 1865.

Dr. Herbert Davies, reviving an old practice, had recourse to free blistering of the inflamed joints, with very satisfactory results.

Such are the chief remedial measures which had been adopted in the treatment of acute rheumatism up to the year 1876. Antiphlogistic treatment, the alkaline treatment, and expectant treatment, are the only ones which have met with anything like general approval.

Antiphlogistic treatment was practised, not because of the proved excellence of its results,—for two hundred years ago these were regarded as unsatisfactory by Sydenham, and have frequently since then been called in question by others,—but because such treatment was the legitimate outcome of the views then held regarding the nature and mode of production of rheumatism.

The alkaline treatment was adopted, not because it had been proved to be specially beneficial, but because such treatment was a therapeutic sequence of the generally accepted acid theory.

The expectant plan of treatment was the practical expression of the opinion which had gradually been gaining ground, that the results of the alkaline treatment were not satisfactory. It succeeded the failure of the alkaline treatment in the nineteenth century, just as in the hands of Sydenham it succeeded the failure of the antiphlogistic treatment in the seventeenth.

A study of the natural history of acute rheumatism led us to the conclusion that the disease is of miasmatic origin, and that the poison which gives rise to it, though specifically distinct, is generically allied to that which causes ague. The ague poison is a minute parasitic organism which finds the nidus necessary to its reproduction in the blood of man. Its morbid action, and the symptoms to which it gives rise, are a result of this reproduction. The rheumatic poison is a minute parasitic organism which finds its nidus in the muscles and fibrous structures of the joints and of the heart, and the symptoms of acute rheumatism result from its reproduction in them.

The adoption of this view of the causation of rheumatic fever opened up a new field of therapeutic research—and a hopeful one too; for of all diseases malarial fever is that over which drugs exercise most control. Quinine cures ague. That is one of the best established facts in the practice of medicine. Rheumatic fever being similar in nature and mode of production there might—nay, there ought to be some drug capable of exercising over its course the same controlling influence that quinine exercises over the course of ague. That is the line of therapeutic research which the miasmatic theory of rheumatism opened up.

A striking fact in the natural history of the malarial fevers is that the trees which provide their cure grow best in countries and localities in which

these fevers most prevail—nature seeming to produce the remedy under climatic conditions similar to those which produce the disease.

In rheumatism a low-lying damp locality and a temperate climate present the conditions most favourable to its occurrence. Looking about for a plant or tree which most flourishes under such conditions, that which most naturally presented itself was the willow—the various species of *Salix*.¹ Among the *Salicaceæ*, therefore, a remedy for rheumatism was sought. The bark of most willows contains a bitter principle called salicin. This seemed exactly what was wanted. If the miasmatic theory of rheumatism were correct, it seemed not improbable that salicin might exercise on the rheumatic poison the same destructive action that quinine exercises on the poison of ague, and might thus cut short the course of rheumatic fever. It was accordingly tried. The results exceeded all expectation. It was in 1874 that the observations were begun; and early in 1876 the results were given to the profession. They were thus summed up:—

“(1) We have in salicin a valuable remedy in the treatment of acute rheumatism.

¹ Besides the *Salicaceæ* another genus of plants, the *Spiraceæ*, also occurred to me as not unlikely to yield a remedy for rheumatism; if the *Salicaceæ* failed, I determined to have recourse to the *Spiraceæ*. They did not fail; but it is to be noted that the *Spiraea Ulmaria*, the common meadow-sweet, contains an oil (*oleum spirææ*) which is salicylous acid, one of the salicyl compounds. With this oil and with a tincture made from the plant for me by Messrs. T. & H. Smith, I made some observations in acute rheumatism. It cured the disease, but the difficulties in the way of administration were too great, and its use was abandoned.

“(2) The more acute the case, the more marked the benefit produced.

“(3) In acute cases its beneficial action is generally apparent within twenty-four, always within forty-eight, hours of its administration in sufficient dose.

“(4) Given thus at the commencement of the attack, it seems sometimes to arrest the course of the malady as effectively as quinine cures an ague, or ipecacuanha a dysentery.

“(5) Relief of pain is always one of the earliest effects produced.

“(6) In acute cases, relief of pain and a fall of temperature generally occur simultaneously.”¹

While these observations on salicin were being made, Kolbe, having discovered a method of manufacturing salicylic acid (originally prepared from salicin) from carbolic acid, was bent on finding some use for it. First tried by surgeons as an antiseptic, it was also freely experimented with by physicians in all sorts of diseases, but chiefly in those attended by fever. Its febrifuge properties were soon recognised, and much that was favourable hoped from, and reported of, its action in typhoid fever, diphtheria, erysipelas, pyæmia, etc. But it was soon seen that the disease in which it did most good was acute rheumatism.

¹ “The Treatment of Acute Rheumatism by Salicin,” by T. J. MacLagan, M.D., *Lancet*, March 1876.

Early in 1876, Stricker¹ and Riess² published a most favourable account of their experience of its employment in that disease. Their results were quite in accordance with those which I had got from salicin.

The conclusions at which he had arrived are thus formulated by Stricker :³—

(1) Salicylic acid appears to be a rapid and radical remedy in recent cases of genuine acute rheumatism of the joints.

(2) It is not injurious to the human organism when administered every hour in doses varying from seven and a half to fifteen grains.

(3) It can be given in these doses for a longer time to young and strong individuals than to the old and feeble.

(4) In the latter, it produces toxic symptoms more readily than in the former.

(5) The toxic symptoms vary in degree.

(6) Those most commonly met with are noises in the ears, difficulty of hearing, and diaphoresis ; when these occur the administration of the medicine should be discontinued.

(7) If salicylic acid be found to fully answer the expectations entertained regarding it, the internal administration of a certain quantity may be expected

¹ *Berliner Klinische Wochenschrift*, Nos. 1 and 2, 1876.

² *Ibid.*, No. 7, 1876.

³ *Ibid.*, 21st February 1876 ; and *London Medical Record*, 15th June 1876.

to prevent the occurrence of fresh attacks in hitherto unaffected joints, and also secondary inflammation of serous membranes, especially the endocardium.

(8) To prevent relapse, the medicine must be continued in smaller doses for some days after the termination of the main treatment.

(9) Salicylic acid is of doubtful utility in chronic articular rheumatism.

(10) It is not likely to be of use in gonorrhœal or diarrhœal rheumatism, or in the polyarthritis attending septicæmia.¹

Results so striking could not fail to attract attention. The new drugs were eagerly tried. Observations were made on all hands. The journals in England, Germany, France, and America contained numerous reports of cases of acute rheumatism treated by salicin and salicylic acid, and very soon it became a matter of general acknowledgment that these drugs possessed in a remarkable manner the power of shortening the duration and controlling the course of that disease. In the year following that in which this method of treatment was brought under the notice of the profession, the leading medical journal in England thus referred to the subject: "There are few practitioners

¹ Previous to the publication of the German reports I had, while making my observations on salicin in 1874 and 1875, tried both salicylic and salicylous acid (*oleum spirææ*), made from the common meadow-sweet. They did good to the rheumatism, but as salicylic acid caused at times unpleasant head symptoms and cardiac depression, and as salicylous acid seemed to irritate the throat and stomach, I abandoned them and stuck to salicin, which gave no unpleasant results.

who have reported themselves as disappointed in the use of this drug; or, to put it at once strongly and carefully, more disappointed than in the use of quinine for ague. There has not been, in fact, such a consensus of medical opinion on any therapeutic question for many years, as on the power of this drug in one form or other to cure rheumatic fever.”¹

The experience acquired during the years that have elapsed since then has amply confirmed the favourable conclusions drawn from the earlier observations, and salicin and salicylic acid are now universally regarded as *the* remedies for acute rheumatism. The evidence, indeed, is now so overwhelming that no one calls in question the efficacy of these drugs, or their power to arrest the course of that disease.

To get its full beneficial effects the drug should be given in full and frequent dose—twenty to thirty grains every hour till the temperature falls and pain is materially diminished. It will generally be found that, when the drug is given in this dose, the pain and fever are materially allayed in eight or ten hours, and abolished within twenty-four hours from the commencement of treatment. It reads like an exaggeration, but it is a strictly accurate statement to say that treated thus by frequent large doses of salicin or salicylic acid, the pain of rheumatic fever is more completely relieved in six hours than under the old forms of treatment it used to be in three weeks. The rapidity with which the

¹ *Lancet*, 8th July 1877.

cure is effected depends on the dose given ; and the necessity for giving the drug in full and frequent dose cannot be too strongly insisted on. Salicin and salicylic acid are rapidly eliminated from the system, and only by giving them in full and frequent dose can their action be kept up. In the early years of this treatment many cases were reported in which these drugs failed to effect a cure. The failures were attributable to the inadequacy of the dose given. To give five or ten grains of salicin or salicylic acid every four or six hours is to do injustice both to the patient and to the drug. Large and frequent doses are necessary—thirty grains every hour till pain is relieved and temperature falls ; after that the interval between the doses may be widened. But to guard against a recurrence of the symptoms it should continue to be administered for ten or twelve days after all pain has ceased.

It is marvellous how speedily the symptoms decline under this treatment. Relief of pain is the first indication of improvement, and this is generally marked before an ounce, often before half that quantity of the drug has been consumed. It takes about an ounce of salicin or salicylic acid to completely allay the acute symptoms, and the sooner this is got into the system the better. The cases are few in which that quantity may not be given, and pain and fever abolished within twenty-four hours of the commencement of treatment ; in many cases this

result is got within twelve hours. So rapid is the cure that it is often difficult to keep the patient in bed for more than two or three days. He should never be allowed to get up within a week; for no matter how completely the pain and fever may be abolished, it must be borne in mind that the structures of the joints have been inflamed, and do not at once resume their normal tone on the decline of the inflammation; time must be given for the effects of the inflammation to pass off, and the inflamed structures to return to their natural condition.

The following cases illustrate the good effects of the salicyl compounds :—

A girl, aged sixteen, never had rheumatism before. Was quite well on 12th April 1875. On the 13th felt out of sorts, and had a general feeling of cold, with some pain in the limbs. On the 14th the pains increased, and towards evening got very bad. She got up on the 15th and went about as usual, saying nothing to any one about her pains, which were severe in both arms and legs. On the 16th she got up, but was obliged to go back to bed.

16th April, vesp. Lies in bed unable to move, and every now and then screaming with pain. The back, shoulders, elbows, wrists, knees, and ankles are all the seat of severe pain, but the knees and ankles are most complained of. All these joints are slightly swollen, and so exquisitely tender that the least touch or movement causes her to scream. Has no pain in

chest. Skin hot, not perspiring; tongue moist and furred; urine scanty, high-coloured, and loaded with pink urates. Has a soft blowing murmur with first sound, loudest at apex, but audible over whole heart. Pulse 112; respirations 20; temperature 103.8° . To have fifteen grains of salicin every hour till three powders are taken, and then one every two hours.

17th, *mane*.—Wandered at times during the night, but had occasional short snatches of sleep. Pain, especially in ankles and knees, is still severe, but not nearly so bad as yesterday. Can move the right leg a little, and does not complain when the joints are touched. Indeed, she allows them to be pretty firmly grasped without complaining; yesterday the least touch made her scream. Tongue furred; skin moist, and perspiration acid. Urine scanty and high-coloured; bowels confined. Cardiac blow is softer in character, and precedes as well as accompanies the first sound at the apex. Still heard over whole heart, but not so distinctly as yesterday. Pulse 96; respirations 26; temperature 102.8° . Has had eight powder—equal to 120 grains of salicin. To continue to take fifteen grains every two hours.

18th, *mane*.—Had a good night, free from pain. To-day feels quite well. Has no pain in any of the joints, and can move the limbs without more discomfort than what is caused by a slight feeling of stiffness in the knees. Tongue cleaning; skin natural. Pulse 72, barely perceptible; respirations 20; temper-

ature $99\cdot6^{\circ}$. Has had eighteen powders, equal to 270 grains of salicin.

19th.—Slept well ; is free from pain, and feels quite well. Wishes to get up. Tongue clean ; skin natural ; bowels moved ; urine abundant, of pale amber colour. Pulse 70, feeble, irregular ; respirations 20 ; temperature $98\cdot2^{\circ}$. Has had in all 405 grains of salicin.

The cardiac blow remained, but gave rise to no subjective phenomena. There was no return of the rheumatism. She went on with the salicin for a fortnight.

Rapid as was the cure in this case—the pain having been practically abolished within twenty-four, and the temperature brought to the normal within, at the most, sixty hours of the time that treatment commenced—it would probably have been still more rapid had the salicin been given in the full dose in which I now administer it. At the time that this case occurred the remedy was still on its trial, and the present certainty regarding the safety as well as the desirability of large doses had not been attained. To such a case occurring now I would give double the dose, and probably with a more rapid result—as in the following case which bore a close resemblance to this one.

A girl, aged seventeen ; had always enjoyed good health. With the exception of measles and scarlatina in childhood, never had any ailment.

On 26th May 1878 she felt out of sorts, and had

such aching in the limbs that she did not leave the house. On the following day she was worse, and towards night got very bad.

28th May.—Lies in bed, unable to move, the least effort to do so causing intense pain, and making her scream. Has anxious pained expression. The knees and wrists are most painful, but the ankles, right shoulder, and neck are also complained of. The affected joints are a little swollen, and exquisitely tender; except over the wrists, there is no redness of the surface. Tongue moist and furred. Skin hot, not perspiring; bowels moved by medicine; urine scanty, and loaded with urates. Heart's sounds normal. Pulse 112; respirations 22; temperature 103°. To have thirty grains of salicin every hour till decidedly relieved.

She began to take the medicine at 6 P.M. Was then in great pain. She felt easier after the third powder; and after the fifth (taken at 10 P.M.) was so decidedly relieved that she fell asleep. Her mother, who remained beside her all night, stated that she would probably have slept on, but that she woke her up to give the salicin at eleven o'clock, and at midnight. After that, she had a powder only every second hour.

29th.—Has a pleased smiling expression. Is quite free from pain, except when joints are pressed; allows one to grasp them, and can move them without more than a feeling of stiffness. Thinks she would have slept all night if her mother had not wakened her to

give the medicine. Perspired a good deal during night. Skin is now covered with acid perspiration: saliva acid; tongue cleaner; pulse 88; respirations 20; temperature 99.8° . Heart's sounds normal. Up to this time (9.30 A.M.) has taken eleven powders, equal to 330 grains of salicin. To have thirty grains every two hours.

7 P.M.—Has had no pain, and says she would like to get up. Complains only of a slight degree of deafness. This her mother noticed before the patient did. Has perspired a good deal; reaction acid. The joints feel stiff when she tries to move them, but can be firmly pressed without pain. Pulse 76; respirations 20; temperature 98° . Heart's sounds normal. Has had in all exactly one ounce of salicin, 16 thirty-grain doses.

She continued to take the salicin in gradually diminishing dose for four days, during which she was kept in bed. At the end of that time she was allowed to get up, and the salicin was given in twenty-grain doses four times a day for a week longer. She made a perfect recovery, and had no return of pain.

In this case the acute pain was abolished within six, and all joint tenderness within twenty-four, hours of the time that treatment commenced. Within that time, too, the temperature had fallen from 103° to the normal standard, a fall of five degrees. The case was a very acute one.

A man, æt. 30, robust and well built, had rheumatic fever for the first time four years ago. Was then two months in bed, and three off work.

31st *December* 1878.—Two days ago was seized with pain in right knee. Yesterday the right was a little better, but the left became very painful. To-day the right shoulder and left ankle are also affected. Of the affected joints the right knee is the only one that is swollen, and it is only slightly so; the other joints are very tender, but none of them red. Had little or no sleep last night from severity of pain. Tongue furred; bowels moved by medicine; urine high-coloured, and depositing pink urates; skin moist, perspiration acid; pulse 100; respirations 22; temperature 101°. Heart normal. To have thirty grains of salicin every hour for six hours; then every two.

1st *January* 1879.—Felt better after four powders, and by night was so relieved that he slept well, waking up only twice—on each occasion taking a powder. Has taken altogether ten of them, equal to 300 grains of salicin. Is quite free from pain. Felt so well this morning that he got up and dressed, and at time of visit was walking about the house. Was ordered to go to bed. In bed is quite free from pain; but when walking about the left knee and ankle hurt. Skin covered with acid perspiration; urine less scanty, of amber colour, with slight deposit of urates. Heart normal. Just after getting into

bed pulse was 88 ; respirations 20 ; temperature $98\cdot8^{\circ}$.
A powder every two hours.

He perspired very freely during the day, and in the evening felt so well that he got up again for a couple of hours.

2nd.—Slept well all night. Took no powder between ten last night and seven this morning. Has had in all eighteen powders, equal to 540 grains. Perspiring freely—secretion acid ; has no pain ; swelling and tenderness quite gone ; pulse 72 ; respirations 18 ; temperature $98\cdot3^{\circ}$. He was ordered to take the salicin three times a day for ten days. He remained well, and resumed work on the 8th of January. In this case the attack was abolished within twenty-four hours.

A man, æt. 34, has twice had rheumatic fever—once at eighteen, and again at twenty-four. On each occasion was laid up for six weeks. Present illness began three days ago with *malaise* and aching in limbs. Pains have steadily got worse, and have become localised in joints.

4th Nov. 1878.—Skin hot ; expression anxious ; tongue furred ; urine high-coloured and scanty ; pulse 116 ; respirations 24 ; temperature $102\cdot5^{\circ}$; ankles, knees, right shoulder, and fingers of right hand are swollen and painful. The heart's sounds are normal. To take thirty grains of salicylate of soda every hour till pain is relieved ; after that, every two hours.

5th.—Is much better. Felt easier after the third dose of the medicine. Had a good night, but perspired a great deal. Is now covered with acid perspiration; saliva is also acid. The swelling is all but gone from the joints; and there is no pain except when they are moved or pressed. Heart normal. Pulse 92; respirations 20; temperature 99·6°. Took the medicine every hour for four hours. He was then easier, and took it every two hours. Has had in all nine doses, equal to 270 grains. Says he feels a little squeamish after it. To take a dose every three hours.

6th.—Feels quite well, only weak. There is no swelling; and no pain even on pressure over the joints. Acid perspiration continues. Pulse 70; respirations 18; temperature 98°. Heart normal.

He remained well, but took the salicylate three times a day for ten days.

A man, æt. 22; never had rheumatism before.

12th December 1877.—Present attack commenced four days ago with sore throat and general aching. Now the pain is localised in left knee, both ankles, and right shoulder. Except the shoulder, the affected joints are slightly swollen, and all are distinctly tender, though the pain is not very acute when he is at rest. Any movement aggravates it much. The skin covered with acid perspiration; tongue furred; urine high-coloured and loaded with fawn-coloured urates; bowels moved by medicine; heart's

sounds normal. Pulse 104; respirations 20; temperature 100.8° .

To have twenty grains of salicylate of soda every hour till pain is decidedly relieved; then every two hours.

13th.—Is much better. Was decidedly relieved after five or six doses of the medicine, but went on with the hourly dose for eight hours. After that he fell asleep, and woke up only now and then during the night. Has had up to this time (11 A.M.) thirteen doses, equal to 260 grains of the salicylate. The joints are stiff and slightly swollen, but the pain is gone. Perspires freely; secretion acid. Pulse 84; respirations 20; temperature 98.8° .

14th.—Pulse 68; respirations 18; temperature 98.2° . Heart normal. Took the salicylate four times a day for four days, and thrice a day for a week more. Remained well.

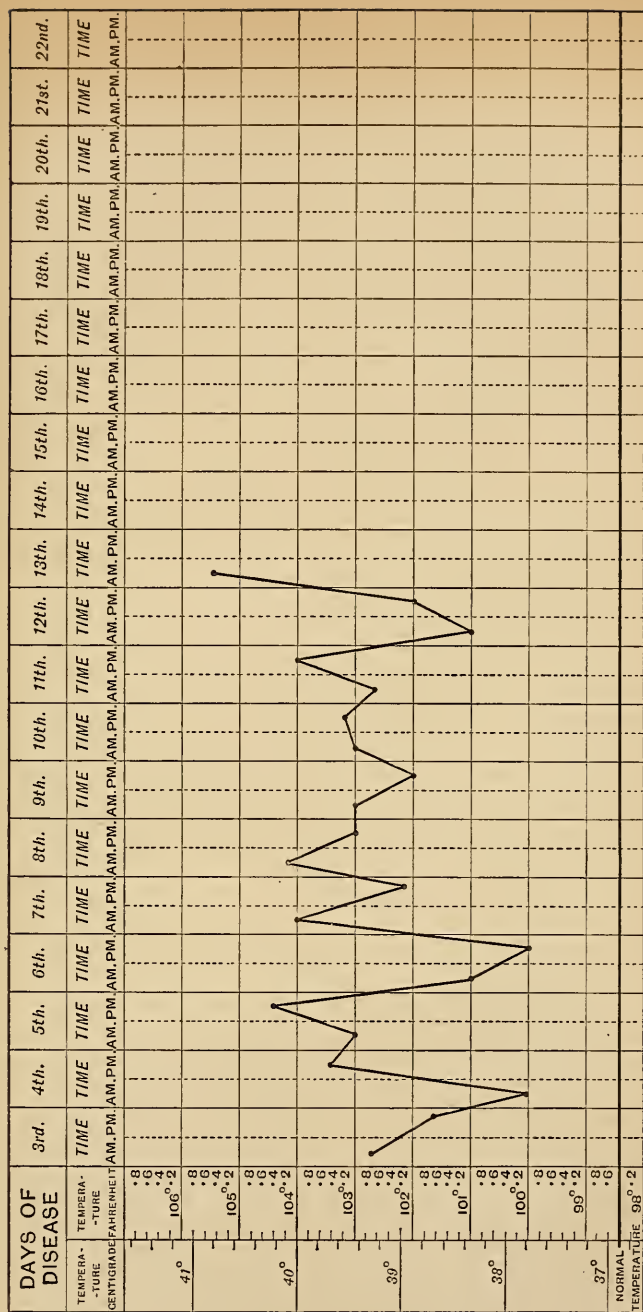
These cases suffice to illustrate the controlling power exercised by the salicyl compounds over the rheumatic process.

In young subjects, and in those who have not suffered from repeated rheumatic attacks, such is generally the course of events, if the remedy is given in sufficient quantity, and for a sufficient time. But it is of importance that these two conditions should be observed; for if given in insufficient quantity the desired result is got slowly or not at all; and if omitted

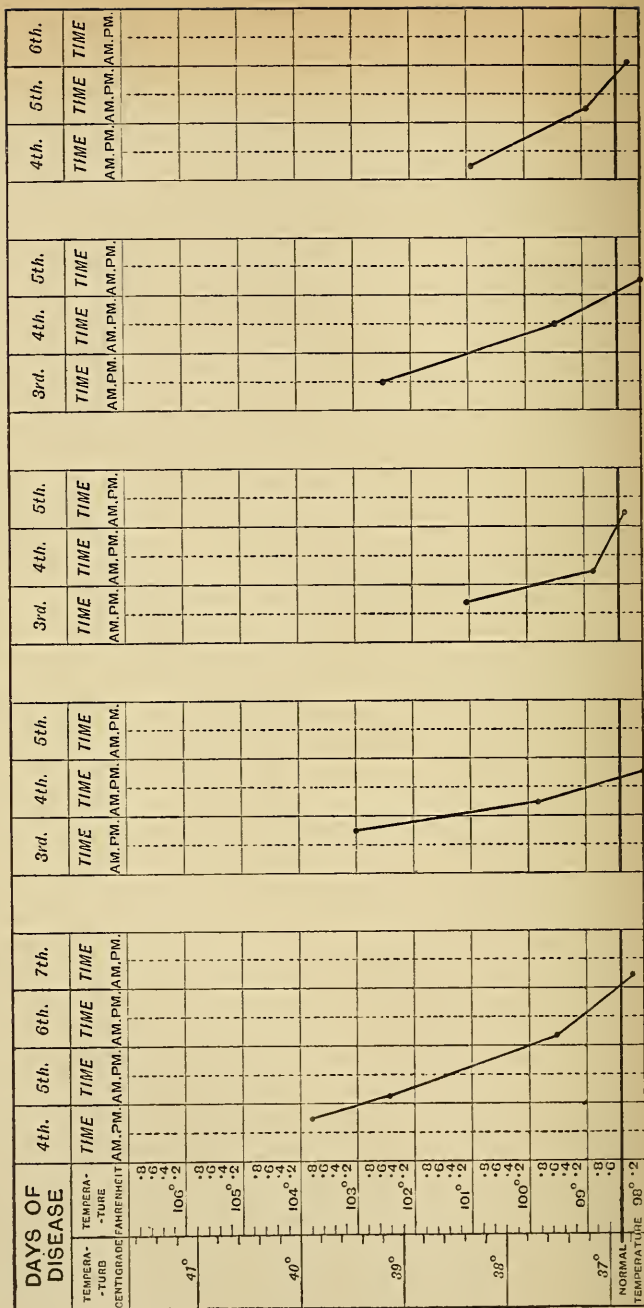
too soon the symptoms are apt to recur. On page 204 is a diagrammatic representation of the range of temperature in these five cases. By way of contrast I have placed on pages 202 and 203 a similar representation of the temperature range of two cases given in Aitken's *Practice of Medicine*—one of Wunderlich's which recovered, and one of Sydney Ringer's which proved fatal. The difference between these two cases and my own five is too striking for comment. These five are fairly representative cases.

It has been said that acute rheumatism is more apt to relapse when treated by the salicyl compounds than when treated by alkalies. It is not so, if this treatment is properly applied. When treated by alkalies, or by the expectant plan, the treatment is continued for several weeks and is omitted when the temperature is normal and pain has ceased. But this result is not due to the treatment. The disease has run its natural course and worn itself out. For that reason there is no tendency to relapse. But when treated by the salicyl compounds the course of the disease is cut short and the temperature falls to the normal standard in a few hours. If treatment be omitted as soon as this result is attained the symptoms are likely to recur, for though the rheumatic process is arrested the rheumatic poison is not all destroyed: what remains is reproduced, and the joint pains and fever reappear. It is not a true relapse, but a

Range of Temperature in a fatal case of Acute Rheumatism, complicated with Pericarditis (Sydney Kinger).



Range of Temperature in five cases of Acute Rheumatism treated by large doses of Salicin or Salicylate of Soda (Mackay).



recrudescence of the symptoms consequent on the too early omission of the drug—a result which may readily be guarded against by continuing the treatment for a time after acute symptoms have disappeared. To effect the complete destruction of the poison and ward off the chance of recrudescence or relapse, the drug (salicin or salicylic acid) should be continued for a week or ten days after all rheumatic symptoms have disappeared. When this is done the complete destruction of the poison is ensured, and the disease does not relapse.

To get the full benefit of the salicyl treatment two things are essential :—

(1) The drug must be given in full and frequent dose till the temperature is normal and pain gone.

(2) It must be continued in smaller dose for ten days after all acute symptoms have ceased.

In the two following cases the too early omission of the treatment was followed by a return of the rheumatic symptoms :—

A woman, aged twenty-five, seen 2nd March 1878, had rheumatic fever five years ago; was then laid up for two months. The present attack began five days ago with *malaise* and pains in the limbs.

2nd March.—Face flushed and anxious; skin covered with acid perspiration; tongue furred; urine loaded with urates; right knee, both ankles, and wrists swollen and very painful. Pulse 104; temperature 102·4°. Heart normal. To have light diet, and

thirty grains of salicin every hour till pain is relieved; then thirty grains every two hours.

3rd.—Took a powder every hour for five hours; after that felt easier, and took one every two hours while awake; has had in all thirteen powders, equal to 390 grains. Is now free from pain; the joints are stiff and slightly swollen, but not tender; pulse 80; temperature 99.8° ; skin covered with acid perspiration; bowels moved; heart's sounds normal. To have a powder every two hours till a dozen are taken; and then one every four hours for a week, and to remain in bed for that time. The patient felt so well that she neglected these precautions; got up on the 5th, and took only an occasional powder after that time. On the 8th the joint pains returned.

9th.—Knees, ankles, and wrists inflamed; acid sweats; pulse 100; temperature 101.9° . To have thirty grains of salicin every hour for six hours; and then every two hours.

10th.—Is free from pain; pulse 76; temperature 98.5° . Has had 360 grains of salicin. To continue it every three hours for four days, and after that, four times a day for ten days. This time she did as directed, and remained well.

In this case there can be no doubt that the relapse was due to the too early omission of the salicin.

What happened was this: The salicin was taken, during the first attack, long enough and in sufficient quantity to arrest the rheumatic process, and destroy

nearly, but not quite, the whole of the rheumatic poison. What remained was reproduced, and gave rise to a renewal of the rheumatic symptoms. On the second seizure, the drug was taken for a sufficient length of time, and in sufficient quantity, to destroy the whole of the poison. Convalescence was, therefore, permanent.

A man, æt. 44, had rheumatic fever when he was twenty-eight years of age, again when he was thirty, a third time when he was thirty-three, and a fourth when he was thirty-seven. On the first occasion he was confined to the house for three months, and was unfit for work for other six, nine in all. The second attack was equally long. During the third and fourth attacks he was in bed for six weeks, and off work for three months. Was always treated by potass.

A fortnight ago he began to suffer from twinges of pain in the back, neck, and right leg. Two days ago got much worse, and was obliged to take to bed. For two nights the pains have been so severe that he has had no sleep.

1st December 1878.—Has anxious expression; tongue furred; bowels confined; skin perspiring; perspiration and saliva acid; pulse 116; respirations 30; temperature 102·1°. Has great pain in left heel, all along right leg, and in knee and hip joints of the same side. The neck, and the right wrist and hand, are also painful and tender to touch. The

affected parts are tender, but not red or distinctly swollen. The breathing seems a little oppressed. The heart's sounds are free from bruit, but are muffled in character; and there is a slight click with the systole. To have an aperient, and thirty grains of salicin every hour.

2nd, mane.—Took a powder every hour till 4 A.M. At that hour he fell asleep, and slept on till eight. Has had up to this time sixteen powders, equal to one ounce of salicin. States that he has no pain, only stiffness of joints and limbs; can bear firm pressure everywhere. Indeed, he felt so well that he got up and at time of visit was sitting in front of the fire, free from pain, but stiff and weak. Skin acting freely; perspiration and saliva acid; pulse 100; respirations 28; temperature 98.4°. States that he can scarcely believe it possible that he is so well. To keep bed, and take thirty grains of salicin every two hours.

Vesp.—Has been quite free from pain; so much so that he neglected his medicine, and went from his room into a cold water-closet. Has no pain; but the pulse is 108, the respirations 30, and the temperature 101°. There is a slight click with the first sound of the heart, but the muffled character of the sounds has disappeared.

To remain in bed, and take a powder every hour.

3rd.—Had a good night; slept from ten till three without waking; felt quite well then; got up and

went to another room to see what o'clock it was; felt weakened and chilled by doing so; slept again from four till seven. Has no pain but feels weak; perspiration abundant and acid; pulse 92; respirations 28; temperature 98.1° . To have salicin (thirty grains) every two hours.

4th.—Passed a very good night, awake only once for a short time; feels quite well; heart's sounds normal; acid perspiration continues; pulse 76; respirations 20; temperature 98.2° .

At this time I ceased to visit him, but gave strict injunctions that the salicin was to be taken in thirty-grain doses every four hours for a week. Five days afterwards, I was sent for to see him again.

Stated that he felt so well that he did not take the medicine regularly, as instructed, but took only half a powder occasionally. Practically the salicin was omitted on the 5th; and on the 7th he put on his clothes and went about the house. On the 8th the pains began to trouble him again.

9th.—Has pain in both ankles and right wrist, all of which are swollen and very tender, but not red. Skin hot, not perspiring; pulse 100; temperature 103.3° . Heart's sounds normal. To have thirty grains of salicin every hour.

10th.—After five powders (150 grains) fell asleep, and passed a good night, waking only once. Pain is gone, only stiffness and slight tenderness on pressure

remaining; heart normal; pulse 100; temperature $102\cdot7^{\circ}$. Continue salicin every hour. Has had 210 grains in all.

11th.—Has scarcely any pain, but feels wretched and out of sorts; the joints are not swollen, but are more or less tender on pressure; perspiration acid, not very abundant; pulse 100; temperature $101\cdot5^{\circ}$. Heart normal. Has had 540 grains of salicin. To have thirty grains of salicin and fifteen of bicarbonate of potass every two hours.

12th.—Is much the same, no special pain; but the tenderness on pressure remains; perspiration slight, but distinctly acid; pulse 100; temperature $101\cdot3^{\circ}$. Continue powders. Has had 750 grains of salicin.

13th.—Feels much better; pain and tenderness gone; pulse 90; temperature 98° . Has taken 930 grains of salicin.

14th.—Feels quite well, only weak; pulse 76; temperature 98° . Has good appetite.

He was more careful on this occasion, remained in bed for a week, took salicin for a fortnight, and made a good recovery without any drawback.

In this case the pain was decidedly relieved within six, and was gone within twenty, hours of the time that he came under notice. The temperature, too, had fallen to the normal standard.

It will be noted that during the first attack, neglect of the salicin, on 2nd December, led to a rise of the temperature from $98\cdot4^{\circ}$ in the morning to 101° in the

evening. Its resumption in hourly doses led to its speedy fall to the normal.

The second attack was clearly attributable to its early omission.

Reference has already been made (at p. 9) to a morbid condition to which the term rheumatism is usually applied, but which is more properly a sequence of rheumatism than a distinct form of the disease. The condition referred to essentially consists in chronic thickening and irritability of fibrous textures which have been the seat of frequent attacks of rheumatic inflammation. The usual history of such cases is that each attack has been less perfectly recovered from, leaving behind it a legacy of increased disability. This history indeed shows, what a knowledge of pathology would indicate, that the textures which have been the seat of inflammation do not recover their natural tone as soon as the inflammation ceases. There remains for a time, which varies with the length and severity of the seizure, some thickening of the fibrous textures of the affected joints, causing the stiffness which is felt after the acute symptoms have disappeared. If the attacks are frequent and obstinate, this morbid change in the fibrous textures is less and less perfectly recovered from; by each succeeding seizure a little more damage is done; and ultimately there is induced a condition of chronic thickening of these textures, which is permanent.

That such a change should take place as a result of frequent and long-continued rheumatic attacks, consists with what we know of the mode of production of similar pathological changes in other organs.

Clinical experience teaches that, when an organ has been the seat of repeated attacks of inflammation, the local symptoms to which such inflammation gives rise are apt to recur in a minor degree from the operation of causes which would not have sufficed to induce the original attack. What more common than for chronic bronchitis to be developed as a sequence of one or more acute attacks; and for the course of the chronic malady to be interrupted by subacute seizures, brought on by causes which would not have sufficed to induce the original malady? A similar instance we have in the readiness with which dysenteric symptoms may be developed in those who have once suffered from the acute form of the disease. Exposure to cold, over-fatigue, mental disturbance—causes which could never have originated the disease—will often bring back some of the local symptoms of the original attack in a milder, but still quite characteristic, form. So it is with fibrous textures which have been weakened and altered by repeated rheumatic attacks. They are rendered irritable and weak by the changes which have taken place in them, and are apt to be disturbed by agencies which have no such effect on healthy fibrous textures. Irritation of fibrous textures, no matter how induced, causes pain

in the affected part. Hence such disturbance as arises in these altered textures from exposure to cold and damp, gives rise to the same symptoms as would result from the action of the rheumatic poison. Originating in true rheumatic attacks, occurring in those who have given decided evidence of being of rheumatic constitution, and characterised by symptoms which are associated with true rheumatism, it is not unnatural that the symptoms should be regarded as due to the action of the rheumatic poison. But such a view is pathologically inaccurate, and pregnant with therapeutic errors. The condition which has to be dealt with is one which, though originally induced by repeated rheumatic attacks, exists, after it has been developed, independently of the cause which gave rise to it.

Pain, swelling, slight rise of temperature, even increased formation of lactic acid, may thus result from inflammation of these altered fibrous textures induced by cold, just as like symptoms would result from similar disturbance set agoing by the rheumatic poison. We may thus have all the symptoms of subacute rheumatism, without any action of the rheumatic poison. Over such an attack the salicyl compounds can exercise no control.

If the subacute exacerbation be due to the action of the rheumatic poison—to a fresh rheumatic attack—the salicyl treatment will do good for a time, but will fail to cure, because the irritable textures will take some time to regain their normal condition,

after the rheumatic poison has ceased to act ; and because the lactic acid formed as a result of their inflammation tends to keep up disturbance in them. Such a case treated by salicin or salicylic acid would be, and with justice, instanced as one in which these drugs gave only partial and temporary relief.

It is in these cases in which the fibrous textures have been the seat of prior attacks of rheumatic inflammation that the alkaline treatment often does good. The change resulting from the former attacks renders these textures more irritable, and more liable to disturbance from the presence of lactic acid. As a consequence of this, the local symptoms are apt to persist for a time after the action of the rheumatic poison has ceased. They are kept up by the lactic acid ; and anything which hastens the elimination of this from the system, tends to shorten the duration of the attack. Hence in such cases the alkaline treatment should be combined with the salicyl. The latter puts a stop to the rheumatic process ; the former aids in the elimination from the system of the lactic acid formed during that process.

As compared with the frequency of the occurrence of the acute and subacute forms of rheumatism in which it originates, this chronic thickening of the fibrous textures is not common, at least in its fully developed form. For this there are two reasons : first, it is only in a minority of cases that the rheumatic constitution is so marked as to lead to attacks

sufficiently frequent and long-continued for its production ; and second, in a large number of those who possess this markedly rheumatic constitution, the heart suffers as well as the joints, and death ensues from the cardiac trouble, before there has been time for the development of permanent thickening of the fibrous textures.

Nowadays, treatment is so successful in shortening the duration of acute and subacute rheumatism, that it may reasonably be hoped that this condition will year by year become less common.

This thickening of the fibrous textures is a condition over which drugs exercise little or no control. As one can never be sure that the pain at a given time may not be due to the action of the rheumatic poison, the salicyl compounds should always be given for a time not with the idea of removing the chronic thickening, but with the object of relieving any purely rheumatic symptoms. For those who can afford it the most useful treatment is such as is to be got at Bath, Buxton, Droitwich, Strathpeffer, and other baths in this country ; at Aix-les-Bains and Dax in France ; at Aix-la-Chapelle, Wildbad, Gastein, Homburg, Wiesbaden, Franzensbad, and other baths in Germany.

Chronic rheumatism is the ailment for which this chronic thickening of the fibrous textures is most apt to be mistaken. Occurring, as it does, in those who have suffered from repeated attacks of acute or subacute rheumatism, and presenting many of the symptoms of

rheumatism, it could scarcely fail to be mistaken for the chronic form. It is of great importance that the two ailments should not be confounded, for their prognosis and treatment are essentially different. Wherein chronic thickening of the fibrous textures consists, its name implies. Its pathology we have just considered. Chronic rheumatism, properly so called, is a very different condition. It is due to the presence and direct action of the rheumatic poison, and is not necessarily, or even usually, accompanied by any perceptible change in the textures involved. It consists simply in rheumatic disturbance of the affected tissue. It differs from the acute and subacute forms—not in nature, but in degree, and sometimes in the special textures involved. It is a true rheumatic attack, in which the morbid process and local disturbance are not sufficiently marked to raise the temperature, or to lay the patient up. The textures involved are the same as those which suffer in the acute and subacute forms, with this difference, that the fibrous aponeuroses and muscles are more apt to be affected.

Chronic articular rheumatism usually affects the same joints as suffer in the acute and subacute forms.

Seldom more than one or two joints are affected at the same time; and in none of them is the pain bad enough to lay the patient up. It shifts from joint to joint, and may last, off and on, for months or even for

years, the patient during the whole time being never really ill, and yet never quite well for more than a few weeks at a time.

The following two cases serve to illustrate this form of the disease :—

A woman, *æt.* 34, the mother of seven children ; had rheumatic fever when she was fifteen. Was in bed for three months at that time. At twenty-seven had a second, but much milder attack, which lasted only for eight or ten days. States that she had been subject to joint pains almost ever since her first attack. Is frequently quite well, and free from pain ; but for last six months has had it very constantly, but never bad enough to prevent her going about.

12th May 1877.—Has been ailing all the winter. For last six weeks has not been out of the house, as going out always made her worse. Has now pain and stiffness of knees, ankles, and wrists ; the last are a little fuller than natural. Heart normal ; pulse 70 ; temperature 98·5°. To have thirty grains of salicin every three hours.

14th.—Feels better than she has done for months. Pain nearly gone. Has taken thirteen powders, equal to 390 grains of salicin.

16th.—With the exception of a little stiffness of the joints, feels quite well. Is free from pain.

A year and a half afterwards she consulted me about one of her children. Told me that the salicin did her so much good that she had taken it, off and

on, almost ever since. Has never enjoyed such good health, or been so free from pain as during the last year.

A man, æt. 35; had an attack of rheumatic fever when eighteen years of age. Was laid up for two months. Has suffered from occasional pains in the joints almost ever since. Thinks he has never been more than three months quite free from pain. Its usual seats are the knees, ankles, and wrists. Generally only one joint is affected at a time. For the last few months the pain has been more troublesome, especially in right knee.

8th December 1878.—Has pain and stiffness of right knee and ankle. Neither joint is swollen, but each is tender on firm pressure. Heart's sounds normal; pulse 74; temperature 98·6°. To have thirty grains of salicin every two hours.

9th.—Feels decidedly better.

11th.—Is free from pain, and more comfortable than he has been for many months. Has had in all 360 grains of salicin.

He continued it three times a day, in twenty-grain doses, for several weeks; and by my advice took it for some months twice a day.

In December 1879 he wrote to me as follows:—
“It is just a year since you prescribed the salicin for me. I thought it might interest you to know that I have continued to take it ever since, off and on. The dose I take is twenty grains once or twice a day.

I have never passed more than a week without it. I was never better in my life than I have been during the past year, and never so free from pain."

The heart is less apt to suffer in the chronic than in the acute and subacute forms; but it does sometimes become involved.

Muscular Rheumatism.—Instead of affecting the joints rheumatism sometimes attacks the muscles and their aponeurotic covering. Its chief seats are the large muscles of the thighs, back, shoulders, and arms. It gives rise to pain in the affected part, increased by movement and pressure. The pain is not so apt to shift about as in the articular form of the malady.

The following cases illustrate this form of rheumatism :—

A woman, æt. 25 ; had for several months suffered, off and on, from pains in shoulders, loins, and right thigh. During the last few weeks they had got worse. Pain is increased by motion. Never had rheumatic fever, or any affection of the joints. She has no other local ailment, but feels weak and out of health. This she attributes to pain and want of sleep. Pulse and temperature normal. To have twenty grains of salicin every two hours till the pain is relieved ; and then three times a day for a fortnight.

Three weeks later she again consulted me. Stated that the powders quite cured her in three days, and that she then omitted them. A week after she

omitted the salicin the pains returned in the old localities. It was again given in twenty-grain doses every two hours for three days; after which time she was ordered to take a powder three times a day for three weeks. This she did; and with the result that the pain disappeared, her general health improved, and she remained well.

A woman, æt. 28; never had articular rheumatism; had suffered for six weeks from pain in both thighs, hips, and lumbar region. Affected parts are somewhat tender to pressure made with the point of the finger, but not to similar pressure with palm of hand. The tenderness is most marked over upper and outer parts of thighs. Has been rubbing on various anodyne and stimulant applications, without relief. Pulse and temperature normal. To have twenty grains of salicin every two hours. On the following day she was decidedly relieved; and on the next, after having taken in all 360 grains, was all but free from pain. She took twenty grains of salicin three times a day for a fortnight, and remained well.

As will be seen from these cases, the treatment of this form of rheumatism is not different from that of the articular form of the disease.

CHAPTER XVI

THE MODE OF ACTION OF THE SALICYL COMPOUNDS

THE salicyl compounds form a numerous and remarkable series. There are in all some thirty or forty substances included in it. The chief of these are :—

	Formula.
Salicin	$C_{13}H_{18}O_7$
Saligenin	$C_7H_8O_2$
Saliretin	C_7H_6O
Salicylous acid (oleum spirææe)	$C_7H_6O_2$
Salicylic acid	$C_7H_6O_3$
Methyl salicylate (oil of winter-green)	$CH_3C_7H_5O_3$
Helicin	$4C_{13}H_{16}O_7 \cdot 3H_2O$
Salicyluric acid	$HC_9H_8NO_4$

Though this table represents not a fourth part of the salicyl compounds, it serves to show the composition of those with which we have to deal. It will be seen that, with the single exception of salicyluric acid, which contains a little nitrogen, they are all composed of carbon, hydrogen, and oxygen.

The basis of the whole series is the radicle salicyl ($C_7H_5O_2$), a substance which has never been isolated.

Salicin is extracted from the bark of various

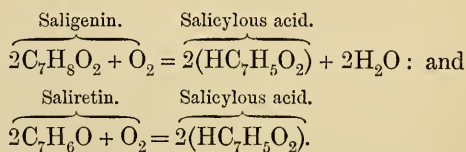
species of willow. It is a white crystalline substance, having a bitter taste. It is sparingly soluble in water.

When boiled for a few minutes with dilute sulphuric or hydrochloric acid, it is converted into glucose and saligenin, which latter may, after agitation with ether, be separated in a crystalline form. The same change takes place when salicin is allowed to remain in a solution of synaptase—the salicin is split up into saligenin and glucose. The solution strikes a deep blue colour with ferric chloride. Salicin itself gives no such colour.

If the boiling with the acid be continued for some time, the saligenin itself is destroyed, and there is formed a resinous substance called Saliretin.

When salicin is acted on by a powerful oxidising agent, such as chromic acid, the change does not stop at the formation of saligenin and sugar. These substances are also decomposed: the sugar producing formic acid, and the saligenin yielding a fragrant oily liquid, which is salicylous acid, or oleum spirææ.

Saligenin and saliretin also yield this oil, when treated with chromic acid. The change which takes place is simply one of oxidation; thus:—



Salicylic acid may be prepared in several ways. From salicin it may be formed by fusing it for some

time with caustic potass. From the oil of winter-green it may also be formed by boiling it with caustic potass for a few minutes. The acid of commerce is prepared from carbolic acid by the action of caustic soda.

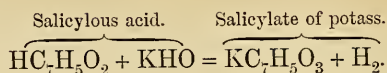
It occurs in needle-shaped crystals, sparingly soluble in cold, but very soluble in hot water. It combines with alkalies to form salts which are much more soluble. It gives a violet reaction with perchloride of iron. When taken into the system, part of it passes away in the urine unchanged, and part becomes converted into salicyluric acid by a process analogous to that by which, under similar circumstances, benzoic acid is converted into hippuric acid. Salicyluric acid also gives a violet reaction with the iron salt. By boiling with concentrated hydrochloric acid, it may be again split up into salicylic acid and glycocine.¹

Salicylous acid exists in nature, in the flowers of the common meadow-sweet, the *Spiræa Ulmaria*; and may be got by distilling these flowers with water. It is generally prepared from salicin by the decomposing action of dichromate of potass. It is a colourless, oily liquid, having a hot pungent taste, and the odour of the flower of the meadow-sweet. It combines with soda and potass to form salicylides. It strikes an intense violet colour with ferric chloride.

If salicylous acid be fused with caustic potass, part

¹ Miller's *Elements of Chemistry*.

of the hydrogen is liberated and salicylic acid is formed :—



The same result takes place when salicylous acid is boiled in an alkaline liquid with oxide of copper.

Salicylous acid is not used in medicine, but special reference is made to it as one of the salicyl compounds, because it is of interest to note that the meadow-sweet (*Spiræa Ulmaria*), from which it is obtained, growing as it does in low-lying damp localities, is the plant to which I had intended to have recourse if the willow had failed to supply what was wanted. I did indeed use in several cases a tincture made for me from its flower by Messrs. T. & H. Smith. It did good to the rheumatism, but the difficulties in the way of its administration, and its pungent taste, led me to abandon it. I have no doubt, however, that an infusion or tincture of the flower of the meadow-sweet would be an effective remedy in acute rheumatism.

As it is, the only two of the salicyl compounds which are used in practice are salicin and salicylic—the former given in powder as it is extracted from the bark of the willow; the latter in the form of salicylate of soda, as prepared from carbolic acid. Both seem to be possessed of the same anti-rheumatic action, but salicin possesses the advantage of having no deleterious action on the system, while salicylate of soda is occasionally found to produce considerable

disturbance of the heart and of the brain—the former showing itself by enfeeblement of the cardiac action, the latter by wandering and delirium, as in the following cases :—

A man, aged forty, who had twice previously, at twenty and twenty-six years of age, suffered from acute rheumatism, had a third attack in June 1878. When seen, on the fourth day of illness, both wrists and the right knee were swollen and painful ; tongue furred ; perspiration acid ; urine high-coloured and depositing urates ; pulse 100 ; temperature $101\cdot4^{\circ}$; bowels moved by medicine ; heart normal. To have twenty grains of salicylate of soda every hour, till six doses have been taken, and after that, every two hours.

He began to take his medicine at noon. In the evening I was sent for to see him. He was better, so far as the rheumatic symptoms were concerned. The joints were less swollen and not so painful ; the pulse was up to 120, and was small and feeble ; the temperature had fallen to $99\cdot8^{\circ}$. But his general condition was much changed. His wife stated that he complained of the medicine making him feel depressed and uncomfortable after the third dose, and that after the fifth he began to wander. When seen by me, after having taken in all 140 grains of the salicylate, he had the appearance of one suffering from delirium tremens. His expression was anxious ; he was wandering, and talking nonsense, fancying that there was some one under his bed, and behind

the window curtains. He knew me perfectly, but, though I was quite alone, asked who it was that I had with me. He had no recollection of having seen me in the morning, and thought that I had come straight to him from Ireland, where I had been some weeks previously. The urine was high-coloured, and free from albumen; he was perspiring freely. The heart's sounds were wanting in tone; there was no abnormal bruit.

The salicylate was omitted, and he was ordered instead thirty grains of salicin every two hours.

On the following morning he was much better. Had wandered during the night, but fell asleep about half-past three; slept for three hours, and afterwards had short snatches. When seen at 9 A.M. was quite rational, but feeling stupid and confused. Had no recollection of having seen me yesterday evening; but quite remembered the morning visit. Pain in joints gone; pulse 100; heart's sounds improved in tone; temperature 98.5° . To have thirty grains of salicin every three hours.

He got rapidly well.

A woman, aged thirty, was laid up with her second attack of acute rheumatism. Right ankle and knee and left elbow swollen and painful; acid sweats; pulse 104; temperature 102.1° ; heart unaffected. She was ordered twenty grains of salicylate of soda every two hours. On the following day, after having taken 180 grains of the salicylate, the rheumatism

was better; the joints were less swollen and scarcely at all painful, except on firm pressure; and the temperature had fallen to 100° ; but the pulse was 120, small and feeble; she complained of nausea, and a sense of misery and depression, and thought the medicine "did not suit her." The heart's impulse was barely perceptible, and the sounds wanted tone. The salicylate was omitted, and she had instead thirty grains of salicin every two hours.

On the following day it was reported that she had slept well all night, having wakened up only twice. On each occasion she took a powder. Took seven in all, equal to 210 grains of salicin. Pain gone; the joints not even tender to touch, but feeling stiff; pulse 96, of better volume; heart's sounds pretty good; temperature 98.8° . To have thirty grains of salicin every four hours. She continued to take it so for several days, and made a perfect and rapid recovery.

A medical friend suffering from subacute rheumatism asked me to see him. He had been taking salicylate of soda which, though it did good to his rheumatism, produced cardiac depression. The following is his own statement: "Both drugs relieved the pain, tenderness, and swelling, when taken in full doses frequently repeated. But the salicylate, which I employed first, produced some very unpleasant effects. After taking several twenty-grain doses, a copious perspiration was produced; the strength of the pulse was very distinctly diminished, while its

frequency was increased; and a feeling of most uncomfortable depression, with singing in the ears, ensued. Indeed, I hardly knew whether the disease or the remedy was the preferable. Salicin, on the other hand, improved the tone of my pulse and digestion, and relieved the pains more rapidly. To my mind, one of the great merits of salicin is the absolute safety with which large doses can be taken. In the course of one period of twenty-four hours I swallowed an ounce of it with nothing but benefit."

Dr. Latham thinks that natural salicylic acid, prepared from oil of winter-green, does not have the same deleterious action as that prepared from carbolic acid. Professor Charteris, who inclines to the same belief, thinks that the special impurity which imparts to the salicylate of soda of commerce its disturbing action on the system is creasotic acid, and that the presence of this noxious ingredient is inseparable from the method of preparing the salicylate. Be that as it may, there can be no doubt that salicin, which is a bitter tonic, does not depress the heart's action as the salicylate of commerce does—a point of much importance in the treatment of an ailment which has myocarditis for one of its complications.

It has been supposed by Senator that salicylic acid is the real anti-rheumatic agent, and that salicin owes its curative effects in acute rheumatism to its conversion into salicylic acid in the blood. More probable is the hypothesis that all the salicyl compounds possess the

power of arresting the rheumatic process, and that they all owe this power to the radicle salicyl, which is the basis of the whole of them. The one which we choose to employ is simply a matter of therapeutic convenience. The two most convenient are salicin and salicylate of soda.

How do they cure rheumatic fever? What is the action by which they arrest the rheumatic process?

Between rheumatic and intermittent fevers there exist not only pathological, but therapeutic analogies. The pathological analogies have already been dealt with. The therapeutic have now to engage our attention.

It is scarcely possible to study the therapeutic effects of the salicyl compounds in acute rheumatism, without comparing them with those of quinine in ague. The analogy forces itself on our notice. Either remedy manifests its effects by a prompt alleviation of all the symptoms of the disease; to ensure its full beneficial action, each has to be given in large and frequently repeated dose, and for some time after the acute symptoms have disappeared; and neither produces the same marked effects in any other ailment. Holding, as we do, that the poisons of rheumatism and of ague, though specifically distinct, are similar in nature and in mode of action; and finding that the morbid process to which each gives rise may be arrested by large doses of somewhat similar remedies, we cannot but regard it as at least probable that the

mode of action of the remedy is the same in both—that the salicyl compounds cure rheumatic fever in the same way that the cinchona compounds cure intermittent.

That the cinchona alkaloids arrest the course of intermittent fever is an established fact in practical therapeutics. How they do so has never been explained. “Ague is the disease of all others in which the power of medicine, both as regards prophylaxis and treatment, is most marked. We know that if a man pass through certain districts, and more especially if he sleep in them, he is likely to be attacked with a fit of shivering which, after lasting some time, will be succeeded by a burning fever, and then by profuse sweating, after which he will feel comparatively well until the next day, when another shivering fit will come on at the same hour, and run the same course as the first. We know that by warning the man against the dangerous locality, or by making him adopt certain precautions, take cinchona alkaloids, if he cannot avoid the place, we may be able to prevent the disease; by administering one large dose of quinine before a paroxysm we may stop its approach, and by continuing the remedy we may prevent its recurrence altogether. But we have no notion of the manner in which quinine counteracts the malarial effects.”¹

¹ *Pharmacology and Therapeutics*, by T. Lauder Brunton, M.D., F.R.S., 1880.

There are two ways in which the curative effects of quinine in ague may be produced : either the quinine may so act on the system as to render it insusceptible to the action of the ague poison ; or it may so act on that poison as to deprive it of its power of affecting the system. In other words, the action of quinine is either on the system, or on the poison. Let us inquire which it is. First, as to its action on the system.

Quinine in large dose (ten to thirty grains) possesses in a remarkable manner the power of lowering the temperature of the body when unduly elevated. How it exercises this power is not known. It has been supposed to be due to a special action of the quinine on the nervous centres ; and if we recognise the existence of a special thermic centre, regulating the production and distribution of heat, as the vaso-motor centre regulates the distribution of the blood, this explanation is a very feasible one.

Binz thinks this effect of quinine is to be explained by its lessening the ozonising power of the blood, and so checking oxidation. All that we really know, and all that concerns us at present, is that quinine in large dose lowers febrile temperature. What we have to consider is, whether or not its curative effect in intermittent fever is due to this property, or to some other and special remedial action.

In virtue of its febrifuge properties, quinine has been administered in all febrile ailments. It was at one time claimed for it that it possessed the power of

cutting short typhus. More recently it has been claimed for it, as for other febrifuge remedies (the cold bath and salicylic acid), that it exercises a distinctly curative action in typhoid fever, and shortens the duration of that malady. But this conclusion is not supported by the evidence. There is no proof that quinine either shortens the duration, or lessens the dangers, of either typhus or typhoid fever; or that it exercises a distinctly curative and curtailing effect in any other form of fever than malarial.

The point is one which could be readily proved; and would long ago have been proved, had the facts been as some have stated them to be.

I have frequently given quinine in large dose in all febrile ailments. My experience entirely coincides with that of Murchison, who says, with reference to both typhus and typhoid fevers, that he had "seen no evidence that, at whatever stage it was given, it shortened the course of the disease or diminished its danger."¹

In intermittent fever the case is very different. Here the quinine actually cures. It puts a stop to the whole morbid process, and all that constitutes the disease; and it does this so constantly, so speedily, and so certainly, and its beneficial effects are so lasting, that one cannot fail to see that they are altogether peculiar, and altogether different from those got from its administration in other febrile ailments.

¹ Murchison, *op. cit.*

That the action of quinine in arresting the course of intermittent fever is not to be explained solely by its febrifuge properties is further shown by its power of preventing such fever. Given during the intermission, it prevents the fever from coming on. It exercises a distinctly prophylactic action. Taken regularly by those living in malarial districts, it prevents them from suffering from the action of the poison of intermittent fever. It exercises no such action in any other febrile ailment.

Besides its febrifuge property, quinine possesses no other special action on the body by which its curative effect in ague can be explained. This property does not account for its remarkable power of arresting the progress, and guarding against the occurrence, of that disease. We are thus forced to the conclusion that the curative effect of quinine in malarial fever is not to be explained by any action which that drug exercises on the system. The only alternative view is that it acts on the poison of intermittent fever, and deprives it of its power of affecting the system.

That poison being a minute organism, there is nothing improbable in the view that quinine should exercise a destructive action on it; for we know from the investigations of Binz that quinine possesses in a remarkable manner the power of destroying many minute organisms. It thus consists both with what we believe regarding the nature of malaria, and with what we know regarding the action of quinine on

minute organisms, that quinine should possess the power of destroying that poison. The exercise of such a power over the malarial poison would amply explain both the prophylactic and curative actions of quinine in intermittent and remittent fever. And there is direct evidence that quinine does thus act on that poison; for in the course of the observations already referred to on Laveran's plasmodium malariae, it has been found that the effect of the administration of quinine is to cause the parasite to disappear from the blood of a man in whose circulating fluid it was readily detected before the quinine was given. The plain inference is that quinine cures ague by destroying the parasite which causes it. Indeed, the evidence in support of this view amounts almost to a demonstration that such is its mode of action.

But, it may be said, if quinine owes its curative effects in intermittent and remittent fevers to its power of destroying minute organisms, why is it only in these maladies that this curative power is manifested? There are many other ailments which are believed to be produced in the same way, but in not one of them does quinine have the same power of arresting the morbid process.

In the natural history of minute organisms there is no fact better established than that such organisms are possessed of specific differences of whose existence their external form gives no evidence. Two organisms may be indistinguishable from each other by the

highest powers of the microscope—so far as can be made out by such examination, they are identical, but it may be found that the one flourishes under conditions which are fatal to the other.

Again, an agency which destroys one organism may have no effect on another, though the two may be apparently identical. A remedy, therefore, which cures one disease by destroying the parasite which gives rise to it, does not necessarily cure all diseases owning a like causation. Hence quinine may cure malarial fever by destroying the organism which produces it, without having a like destructive effect on the organisms which give rise to diphtheria, small-pox, scarlatina, typhoid fever, etc.

Minute organisms possessed of specific differences may have these differences manifested, not only by the different effects which they produce on the system, but by the different effects which other agencies have on them. The fact that quinine does not shorten the duration of all diseases caused by the propagation of minute organisms in the system, is no proof that it does not owe its power to cut short intermittent fever to a destructive action on the organism which gives rise to that malady. The fact that it does cut short this fever, is to be accepted as a hopeful indication that other remedies may be found capable of exercising a similarly beneficial effect on other forms of fever whose course we are now powerless to control.

It is, indeed, in the recognition of this view—that

the curative effect of a drug may be due to its action on the poison of the disease, rather than on the system in which it occurs—that lies the main hope for the future discovery of remedial agencies, calculated to arrest the course of maladies which owe their causation to the propagation of minute organisms in the system.

One of the practical results of the study of the natural history of such organisms has been the recognition of the existence of agencies which exercise a destructive action on them. The recognition of such agencies, and of the possibility of dealing with diseased processes, and actually curing disease, by means of drugs which do not necessarily have any action on the system—which act not on the sufferer but on that which makes him suffer—the recognition of such a possibility marks an epoch in therapeutics, and opens up a vast and interesting field of research.

We know that the poisons which give rise to typhoid fever, scarlet fever, measles, and other allied maladies are minute organisms which are largely reproduced in the system during the course of the maladies to which they give rise, and whose morbid action is intimately associated with their organic reproduction in the system. The ideal method of treating these maladies (an ideal which may some day be attained) would be to cure them by destroying the poison which gives rise to them, by administering to the sufferer something which, while it had no

injurious effect on him, would kill the parasite which was making him ill. In malarial fevers the ideal is the same—only here it has been attained. That it has been attained in one disease should make us hopeful of getting like good results in others.

It was the belief (1) that the rheumatic poison is allied in nature to that of intermittent fever; (2) that each is a minute organism; (3) that the morbid effects of each are due to its propagation in the system; (4) that the curative effects of the cinchona compounds in intermittent fever are attributable to their destructive action on the poison of that disease—it was this belief that led to the inference that salicin might exercise a like destructive action on the poison of rheumatism. If quinine destroyed the poison of intermittent fever, it seemed, for reasons already given, that salicin might exercise a like destructive action on that of rheumatism, and a like curative effect on the disease to which it gave rise. That it does produce this curative effect has been abundantly demonstrated.

All that has been said regarding the action of the cinchona compounds in ague is, *mutatis mutandis*, applicable to the action of the salicyl compounds in rheumatism. The analogies which are believed to exist between the poisons of intermittent and of rheumatic fever have already been pointed out.

Between the cinchona compounds and the salicyl compounds there are also marked analogies.

(1) The most prominent of these is the power which each possesses of curing a miasmatic fever. The cinchona compounds cure intermittent, the salicyl compounds cure rheumatic fever.

(2) The cinchona compounds are possessed of no physiological action by which their power to arrest the course of intermittent fever can be explained. It is the same with the salicyl compounds. On the non-febrile body they have no action by which their curative effects in rheumatic fever can be accounted for.

(3) It was at one time hoped, and has been at various times asserted, that quinine would arrest the course of other fevers than intermittent and remittent. But though it has been established that quinine in large dose lowers the febrile temperature, often several degrees, it has been equally established that this effect is only temporary, and that the only fevers in which it exercises a distinctly curative action are intermittent and remittent. It is the same with the salicyl compounds. It has been hoped, and over and over again asserted, that they possess a curative action in the same febrile ailments over whose course quinine was at one time believed to exercise a controlling influence. But the result has been the same as with the cinchona compounds. Though the salicyl compounds have been proved to be possessed of febrifuge properties, they exercise no distinctly curative effect in any febrile ailment

except acute rheumatism. As febrifuges they are much inferior to quinine. I have frequently seen a couple of ten-grain doses of quinine, given the one an hour after the other, lower the temperature three or four degrees, after several hourly thirty-grain doses of salicylate of soda had failed to have any effect.

But though the salicyl compounds possess the febrifuge property to a less extent than the cinchona compounds, they are not devoid of it. And we have now to inquire whether or not their beneficial action in acute rheumatism is due to this or to some other special curative effect.

It is with the salicyl compounds in rheumatism as with the cinchona compounds in ague—there are but two ways in which their remedial action can be explained. Either they so act on the system as to render it insusceptible to the action of the rheumatic poison; or they so act on the rheumatic poison as to prevent it from acting on the system. First, as to their action on the system.

Like quinine, the salicyl compounds have no effect on the temperature of the non-febrile body, but possess, in an undoubted manner, the power of lowering that of the febrile body. To produce this antipyretic effect, they require to be given in much larger dose than quinine; and even then their action is less certain and less decided than that of the cinchona alkaloid. Riess has maintained that sali-

cylic acid shortens the duration of typhoid fever. I have given it freely in both typhus and typhoid fevers, and never found any evidence that it either shortened the duration or diminished the mortality of either of these maladies. This seems to be the experience of most observers. Were Riess right on this point, the accuracy of his statement would have been placed beyond doubt before now; for salicylic acid was freely used in typhoid fever before it was given in acute rheumatism. Its remedial power in the latter has been matter of demonstration for twenty years. Its remedial power in the former has yet to be demonstrated; and evidence is every day accumulating to show that Riess erred in attributing such an action to it.

Evidence all tends to show that though the salicyl compounds are possessed of undoubted febrifuge properties, there is but one febrile ailment in which they are known to exercise a distinctly curative effect. In other fevers they may for a time lower the temperature, but they do not materially alter the course or curtail the duration of the malady. In rheumatic fever alone they put a stop to all that constitutes the ailment—the local inflammation and pain, as well as the general febrile disturbance.

Rheumatic fever does not consist solely of fever. An essential part of its existence is inflammation of the fibrous textures of the joints. Just as it is

impossible for any poison to produce the disease without causing inflammation of these textures, so it is impossible for any remedy to cure it without allaying that inflammation.

In considering the curative effects of the salicyl compounds in this disease, attention has been directed too much to the rapidity with which the temperature has been reduced and not enough to the equally great, or even more marked, rapidity with which the joint inflammation is arrested. Indeed, the arrest of this, and the speedy relief of the suffering to which it gives rise, constitute the most striking of the effects of the salicyl compounds in rheumatic fever. A man may be screaming with agony and unable to move arm or leg without the most acute suffering, the joints swollen and inflamed, and his condition one of intense misery. Salicin or salicylic acid is administered in thirty-grain doses every hour, and in eight or ten hours the pain is gone, the joint inflammation is arrested, the man can move his limbs, and the joints can be handled without causing discomfort. No febrifuge action can explain this. No remedy which simply allayed fever could give such a result.

In the whole field of practical medicine we know nothing like it. There is no other instance in which acute inflammation of any structure is arrested with the rapidity with which the salicyl compounds subdue acute rheumatic inflammation

of joints. And the joint inflammation of acute rheumatism is the only form of inflammation over which the salicyl compounds exercise this controlling influence. Their curative effects are not due to their febrifuge properties; for in no other fever than rheumatic do they lower the temperature permanently. They are not due to any power of arresting the process of inflammation, for only in rheumatic inflammation is their curative action got; and yet in acute rheumatism they rapidly subdue fever and arrest inflammation of the joints. They put a stop rapidly and effectively to the whole process of acute rheumatism, and they do this without having the power to arrest any other morbid process. Clearly their action is essentially anti-rheumatic. They act not on the system, not on the joint tissues, but on the rheumatic poison. The symptoms of acute rheumatism are all due to the propagation in the system of the organism which constitutes the poison of the disease; the salicyl compounds arrest these by destroying that poison.

The rapidity with which the disease is arrested resembles the crisis of a fever more than anything else. The crisis of a fever means the cessation of the action of the poison which causes it. The rapid decline of the symptoms of acute rheumatism under the influence of the salicyl compounds means the same thing—the cessation of the action of the

rheumatic poison. In both cases the cessation of the symptoms is somewhat abrupt: in the one case the poison ceases to be reproduced because the material necessary to its reproduction is exhausted; in the other the poison ceases to be reproduced because it is destroyed.

CHAPTER XVII

THE ACTION OF THE SALICYL COMPOUNDS IN THE HEART COMPLICATIONS

IN its general pathology, rheumatism of the heart is identical with rheumatism of the joints. The poison is the same; the textures which chiefly suffer are the same; and there is no difference in the mode in which the poison acts. The morbid process is, therefore, fundamentally the same in both.

Such being the case, it is natural to suppose that both should yield to the same treatment, and that the beneficial results which follow the administration of the salicyl compounds in rheumatic inflammation of the joints, should equally follow their administration in similar inflammation of the heart. And such no doubt would be the case, if the heart were in all respects similarly situated to a joint. But it is far from being so; for though in its pathogenesis rheumatic inflammation of the heart does not differ from rheumatic inflammation of the joints, there nevertheless are several points in which they show divergences—several peculiarities pertaining to each—which must be recognised if we would form a just

estimate of the relative value of the salicyl compounds in the treatment of each.

In both heart and joints it is the fibrous textures which suffer first and chiefly. In both heart and joints these textures have the same duties to perform, the same sort of work to do. The chief difference to be noted between them is in their relative functional activity. A joint acts only occasionally, never for more than a few hours in succession, and gets complete rest for many hours every day. The heart gets no rest, but beats on by day and by night without cessation or repose. This physiological difference exercises a vast and important influence in disease, and especially in such acute inflammation as that which now engages our attention.

To an inflamed organ rest is of the utmost importance. If a joint is inflamed it becomes painful; motion increases the pain; instinctively we give it rest, and its function is in abeyance till the inflammation is at an end. If a man suffering from rheumatic inflammation of the knees and ankles were to persist in going about as usual (supposing such a thing to be possible), he would thereby prevent recovery. The salicyl compounds might be given so as to destroy the rheumatic poison, but the continued exercise of the inflamed textures would keep up the inflammation, independently of the cause which originally set it agoing, and they would probably not recover till they got rest.

When the heart is inflamed, it gets no rest: no matter what the consequences to itself, its work has to be done; and done it is, so long as life lasts. The fever of the accompanying joint affection, as well as the inflammation of its own textures, causes increased excitability and increased frequency of action, so that, instead of rest, there is greater activity—instead of function being in abeyance, it is exalted. This it is which makes the chief difference between the results of rheumatic inflammation of the heart, and similar inflammation of a joint, and makes the heart inflammation so much less amenable to treatment. In both heart and joints the rheumatic poison causes inflammation and consequent thickening of the fibrous textures. In the joints the inflamed structures get complete rest; under proper treatment the inflammation rapidly subsides, its products are quickly got rid of, and the affected structures soon resume their normal condition. But in the heart rest is unattainable—the favourable conditions so easily got in the case of the joints are not to be had, and the results of the inflammation are, therefore, more lasting. It is not so much in the nature of the morbid process as in its results that lies the difference between rheumatic inflammation of a joint and rheumatic inflammation of the heart; and the main factor in producing this difference is physiological rest, easily got in the joints, unattainable in the heart. In considering the question of the respective amenability to treatment of the joint in-

flammation and the heart inflammation, it is essential that this should be borne in mind. The destruction of the rheumatic poison must put a stop to its direct action on the heart as well as on the joints. But to do this is quite a different thing from removing the morbid products resulting from that action. It is a step, and a very necessary one, towards that end; but something more is requisite to its complete attainment. For this it is important that the inflamed textures should have rest. This is readily got in the joints, but not in the heart. The inflamed valves continue to be strained, their roughened surfaces continue to rub, the friction keeps up the irritation, and restoration to the normal is thus rendered difficult, in many cases impossible.

If the heart suffer, it does so for the same reason that a given joint suffers—because its textures are a nidus for the propagation and action of the rheumatic poison. If the heart contain this second factor, it does so naturally and before the rheumatic poison gains entrance to the system. It is, therefore, in danger from the very first; and, theoretically, there is no reason why it should not give evidence of disturbance at as early a period as the joints. Practically, there are two reasons why it should not do so:—

- (1) The joints are much more numerous; and the chance of one or more of them suffering first is correspondingly great.

- (2) The symptoms of rheumatic inflammation of

the fibrous textures of a joint are prominent from the commencement of the attack ; those of rheumatic inflammation of the fibrous textures of the heart are more tardily developed, and are not apparent till these textures have suffered for some time.

Let us consider this second point carefully, for it is an important one.

In both joint and heart the fibrous tissue is the part which suffers first. In the joint the inflammation extends from the fibrous textures to the synovial membrane ; in the heart, from the fibrous rings and valves to the endocardial lining. Before the synovial membrane becomes affected, there is already pain, tenderness, and all the evidence of inflammation of the fibrous textures. But until the mischief has extended to the endocardium there is no evidence, and no possibility of diagnosing the existence, of inflammation of the fibrous textures of the heart ; for such inflammation gives rise to no symptoms or signs until some change has taken place in the membrane.

The signs of valvular endocarditis (to which for the present we shall confine our attention) are those of roughening of the endocardial surface of a valve ; but such roughening is not produced by the direct action of the rheumatic poison on the lining membrane ; it results from friction of the valvular surfaces consequent on a prior inflammatory thickening of the subjacent fibrous textures. It follows from this that there is a stage of the endocarditis which precedes the roughen-

ing of the endocardial surface—precedes, that is, that change which gives rise to the earliest evidence of the heart affection. This stage consists in inflammation and proliferation of the cellular elements of the deeper fibrous structure of the valve. Inflammation in the fibrous structure of a valve does not cause pain as it does in the fibrous textures of a joint—indeed, it gives rise to no symptoms. The earliest evidence of the occurrence of endocarditis—that by which we diagnose its existence—is the development of an endocardial murmur; this is caused by roughening of the valvular surface; but this roughening comes on only at a comparatively late stage of the endocarditis; for the valve is already swollen from the action of the rheumatic poison before there begins the rubbing of their swollen segments which is the direct cause of the roughening. Hence rheumatic endocarditis cannot be diagnosed till the ailment has existed for one or more days. An endocarditis whose physical signs first become apparent on a Wednesday, has almost certainly begun on Monday or Tuesday. If the rheumatic poison affect a joint and the heart simultaneously, pain, the earliest evidence of joint inflammation, will precede, possibly by some days, the endocardial blow which is the earliest indication of the heart being affected. The rapidity of development of the endocardial murmur will vary with the acuteness of the attack; but in any case, its comparatively late development will make the cardiac

inflammation appear secondary to that of the joints, though the two may in reality have originated simultaneously. The point is, that while rheumatic arthritis is diagnosed as soon as it occurs, rheumatic endocarditis cannot be diagnosed in its earlier stages.

Keeping before us these special peculiarities of rheumatic inflammation of the heart, we are in a position to take up the important question of the action of the salicyl compounds in such inflammation.

The question has naturally two aspects—a prophylactic and a curative.

(1) Do the salicyl compounds tend to prevent heart complications in acute rheumatism?

(2) Do they have a curative action on these after they have occurred?

We shall first deal with the prophylactic aspect of the question.

That a remedy which rapidly cures acute rheumatic inflammation of the joints should tend to ward off, if not prevent, the heart complications which so frequently accompany such inflammation, is a reasonable supposition.

If it be the case that rheumatic inflammation of the heart is produced in the same way as rheumatic inflammation of a joint; and if it be the case that the salicyl compounds destroy the rheumatic poison, should not these compounds, in virtue of that action, ward off and arrest the course of heart inflammation, as they ward off and arrest the course of inflammation

of the joints? Theoretically, yes; practically, no. And "no" for the following reasons.

The earliest evidence of the existence of endocarditis is the development of an endocardial murmur. But we have seen that the roughening of the valvular surface which gives rise to this murmur marks a comparatively late stage of the endocarditis, and that before it can occur there must be:—

(1) The reproduction of the rheumatic poison in the fibrous structure of the valve.

(2) Proliferation of the cellular elements of that structure.

(3) Swelling and thickening of the fibrous structure, and consequent bulging of the endocardium over the seat of the swelling.

(4) Rubbing of one swollen segment against another.

(5) Roughening of the endocardial surface, as a result of this rubbing.

It is not till all this has taken place that a murmur is developed or a diagnosis made. So that the rheumatic poison has been exercising its action on the heart for one or two days before there are any signs of its doing so.

If the salicyl compounds be given to a man just as the fibrous textures of the heart are beginning to suffer, they are not given in time to stop the action of the rheumatic poison on them, or to prevent proliferation of their cellular elements; they are not given in time, therefore, to prevent swelling of the valves, and rubbing of their segments, and, conse-

quently, not in time to prevent those changes on the endocardial surface to which that rubbing gives rise.

The development of an endocardial murmur after the commencement of the salicyl treatment, seems to indicate that this treatment possesses no power to prevent cardiac complications. More careful inquiry shows this conclusion to be hasty, and probably erroneous. For, first, the signs of endocarditis are not developed till the disease has already existed for one or two days; and, second, as we know from what is observed in rheumatic inflammation of the joints, it takes another day to get the full action of the salicyl compounds. A man may begin to take these compounds on Monday, and on that day the heart's sounds may be quite normal. On Tuesday his joint inflammation may be much better, but there may be a distinct endocardial blow. From the coincident decline of the arthritic and development of the cardiac symptoms the inference might naturally be drawn, and has in several cases been drawn, that the salicyl compounds, though they cure the joint inflammation, have no power to prevent cardiac complications in rheumatism. But a careful examination of all the circumstances of the case would lead to a more cautious, if not different, conclusion.

Any prophylactic property possessed by the salicyl compounds in rheumatic inflammation of the heart must be due to their destructive action on the rheumatic poison. But this saving action cannot be got

unless they are given in adequate quantity before the poison has begun to act on the heart; for with the commencement of morbid change in that organ terminates the period of possible prevention.

But even if the start were fair and equal—even if the salicyl treatment commenced at the same moment that the rheumatic poison began to act on the fibrous textures of the heart—the morbid process would still have the advantage, for probably twenty-four hours would elapse before there could be introduced into the system the quantity of the salicyl compounds requisite to the destruction of the poison. During these twenty-four hours the rheumatic poison would have time and opportunity to cause such change in the fibrous textures as would lead to thickening of the valves, to consequent rubbing of their segments, and to the development of the symptoms of endocarditis; while the continued activity of the inflamed tissues would prevent the decline of the inflammation, which might otherwise be expected to follow the destruction of the rheumatic poison.

It has been abundantly proved that the salicyl compounds do possess the power of arresting and cutting short the course of rheumatic fever. This means that they possess the power not only to allay the inflammation which already exists, but also to prevent that which would certainly arise, either in those joints which have already been affected, or in others, if the attack were prolonged. If we admit

their power to prevent rheumatic inflammation of the joints, we cannot but accord to them the power to prevent similar inflammation of the heart. Indeed, if the view which has been advanced as to their mode of action be correct, they cannot fail to prevent cardiac complications, if only they are given in sufficient quantity to destroy the rheumatic poison before this has begun to affect the heart. The chief obstacle to their doing so is the early stage at which the heart is apt to suffer. It is only in a minority of cases that time and opportunity are given to get the full action of the salicyl compounds before the heart is affected. This is specially the case in hospital practice, in which the patients seldom come under notice before the disease has existed for the best part of a week.

The very acute cases which come under observation during the first two or three days of the illness are also the ones in which the heart is apt to be affected from the commencement. In such cases the joint and heart affection are often contemporaneous, though, for reasons already given, the symptoms of the heart trouble are more slowly developed.

In subacute cases the symptoms are developed less rapidly, and the heart affection is more likely to be delayed a few days; but so also is the period at which treatment commences, for such cases are generally ailing for at least three or four days before they come under notice.

In acute cases the heart affection is developed so

soon and so quickly that there is not much time to get the prophylactic action of the salicyl compounds. Subacute cases come under notice at so comparatively late a period that there is not much opportunity to do so. So that whatever prophylactic action we may accord to the salicyl compounds on theoretic grounds, there remains the difficulty that in many cases this action is not readily got. There can be no reasonable doubt, however, that it may be, and is actually, got in some cases; for a remedy which so quickly arrests the course of acute rheumatism, and so shortens its duration, cannot fail to diminish the risk of complications arising during its course. A case of rheumatic fever, in which treatment is begun on the third day, is practically cured by the fifth if the salicyl treatment is properly carried out. It is thus saved from all the troubles and possible complications which might arise after the fifth day if allowed to run its normal course of three or four weeks. Among these possible complications endocarditis occupies a prominent place; for though heart complications generally occur during the first few days, they may arise at any time during an attack of acute rheumatism.

With such a possibility before us, and with such a tremendous issue at stake, it is impossible to exaggerate the importance of the early and free administration of the salicyl compounds in all cases of acute and subacute rheumatism; for we never know when we may be dealing with a case in which

prophylaxis is attainable. The bare possibility of such a result is worth striving for. But promptitude and decision are requisite to success. Thirty grains should be given every hour till the temperature is normal and pain gone. A delay of a few hours in commencing treatment, or the administration of the drug in insufficient dose, may make all the difference between perfect recovery, and recovery with a damaged heart—a calamity which, in some cases, is scarcely preferable to death, so hard may be the conditions under which life is carried on.

Do the salicyl compounds have a curative action in rheumatic inflammation of the heart?

Regarding such inflammation as identical in nature and pathology with rheumatic inflammation of the joints; and recognising the distinctly curative effect of the salicyl compounds in the latter, it might, not without reason, be expected that they should have the same action in the former—that they should cure rheumatic carditis as they do rheumatic arthritis. Experience, however, has shown that such is not the case; and that under the salicyl treatment, as under all others, rheumatic endocarditis (to which we shall still confine our attention) is apt to leave some trace behind.

Attention has already been drawn to one obstacle which intervenes to make the treatment and cure of inflammation of the heart specially difficult—the

impossibility of giving rest to the inflamed textures. This is an obstacle which no treatment can overcome. It is an important factor in keeping up the mischief originated by the rheumatic poison, and affords an adequate explanation of the fact that the treatment which allays acute rheumatic inflammation of a joint may fail to have a like action in similar inflammation of the heart. In both rest is essential to quick recovery. In the one it is easily got, in the other it is unattainable.

But it is not enough to explain why the ailment should be so little amenable to treatment during its acute stage. We have also to explain why the endocardial mischief is so apt to be lasting.

Pericarditis may be perfectly recovered from, the effused products may be absorbed, and the membrane restored to its natural state. So, too, may myocarditis. But in endocarditis the signs are more apt to persist after all inflammatory mischief has ceased. It is a pathological fact that when once a certain amount of change has taken place on the endocardial surface, the damage is apt to be irremediable and permanent. The endocardium is the only structure habitually affected by the rheumatic poison of which this can be said; it is also the only structure in the heart which has no analogue, anatomical or physiological, in the joints. The fibrous and muscular textures of the heart and joints have a like structure and function. So have the pericardial and synovial

membranes. So that everything which recovers in a joint may recover also in the heart. The endocardium alone is unrepresented in a joint. It stands alone, too, in its pathology. Its scanty vascularity and low vital activity make it insusceptible to acute general inflammation; such inflammation is, therefore, unknown in connection with it. The same circumstances intervene to prevent the absorption of products effused on its valvular portion during an attack of rheumatic endocarditis. To the absorption of such products a certain degree of vascularity is necessary; such vascularity does not exist in the endocardium, and, therefore, lymph deposited on its surface is not readily absorbed.

It may, indeed, be said that a degree of vascularity which suffices for the effusion of lymph, should suffice also for its absorption. But the deposit on the valves is not all effused. Part of it is deposited directly from the blood on the roughened surface; and even the primary roughening results from irritation caused, not directly by the rheumatic poison, but by friction of the valvular surfaces—a mechanical force which, in the case of the heart, cannot be equalled or counterbalanced by any agency which stimulates absorption.

It is evident that the condition is one on which drugs can have no direct action, and thus is explained the inability of the salicyl compounds to repair the damage done during an attack of rheumatic endocarditis.

The direct cause of all the objective, and most of

the subjective, symptoms of endocarditis, is not the rheumatic poison which causes the inflammation,—it is not even the inflammation itself,—it is the physical change caused by the rubbing and roughening of the swollen valves. All that the rheumatic poison does is to cause inflammation and thickening of the fibrous texture of the valves, and all that the salicyl compounds can do is to cure this. But the symptoms of endocarditis are due not to this but to roughening of the endocardial lining of the valve, which is an indirect result of the valvular thickening. Its direct cause is friction. Over this the salicyl compounds can exercise no control. But the fact that they are powerless to remove such damage becomes an urgent reason for doing our utmost to get the system under their influence, and out of that of the rheumatic poison, before the heart becomes involved.

But though they fail to effect a cure in all cases, there can be no doubt that they do so in some. I am quite sure that I have seen many more cases of complete recovery from rheumatic endocarditis under the salicyl treatment than under the alkaline treatment which it replaced. Under the old treatment one did not expect it; under the salicyl treatment I have come to regard complete recovery as quite an ordinary occurrence.

The destruction of the rheumatic poison cannot fail to have an ameliorating effect on the cardiac inflammation of which that poison is the cause.

But this is not the only way in which the salicyl compounds tend to mitigate the severity of the heart affection. Under their influence the joint inflammation subsides, and the febrile disturbance is allayed. This result is accompanied by diminished frequency of the heart's action. The cardiac pulsations may fall from 112 to 72—a fall of 40 a minute, 2400 an hour, or 57,600 a day. This diminished frequency of the heart's action implies decreased functional activity of the inflamed textures; and this quieting of the heart's action is the one condition which is most desired, and most difficult to attain, in the treatment of rheumatic inflammation of the heart.

Were the rheumatic process not thus cut short, the rheumatic poison would continue to act for some weeks; the heart would continue to beat at the rate of 112 per minute, if not more; the inflamed valves would every day be subjected to the strain and rubbing involved in their action 57,600 times more frequently—an enormous difference which could not fail to tell injuriously.

It is evident that, independently of the good which must directly result to the heart from the destruction of the rheumatic poison, and the consequent cessation of its action on the cardiac structures, benefit must accrue to that organ from the diminished frequency of its own action consequent on the arrest of the joint inflammation and accompanying fever.

The general conclusion to which we are led is that

the early and free administration of the salicyl compounds is likely to ward off cardiac complications, if only the system is brought under their influence at an early period of the attack and before such complications occur, and that it mitigates the severity of these when it is too late to prevent them. Even when the heart's structures are affected, the prospect of complete recovery is, under the salicyl treatment, much more hopeful than under any other; but to attain such a result not only must the treatment be continued for a fortnight after the acute symptoms have passed off, but the patient must be kept quiet in bed for two or three weeks more; the object being to keep the heart as quiet as possible so as to aid the return to their normal condition of the inflamed and thickened fibrous textures. In helping to keep the heart quiet digitalis is often of service.

The general treatment applicable to rheumatic inflammation of the heart is thus the same as that which is applicable to similar inflammation of the joints. The existence of heart complication in a case of acute rheumatism is not only no reason for omitting the salicyl compounds, but is an additional one for giving them freely, and in large dose.

In the great majority of cases no other treatment is required. But every now and then a case occurs in which considerable benefit is got from the adoption of local measures.

In pericarditis especially local treatment is some-

times of much importance. In the early stage of a severe attack, when pain is a prominent symptom, when the heart's action is disturbed and tumultuous, and when there is evidence of serious interference with the circulation, much good may be got by abstracting a few ounces of blood. This may be done by opening a vein, or by the application of leeches, or cupping-glasses, over the region of the heart. If the symptoms are urgent, venesection affords the most speedy relief; but to do good it must be had recourse to at an early stage. The cases are few, however, in which the desired effect may not be got from leeches.

In entertaining the question of bleeding, local or general, it must be borne in mind that the acute stage, when got over, is followed by one in which there is apt to be considerable depression and debility. If bleeding be had recourse to unnecessarily, or too freely, this stage will be rendered more marked and prolonged. The mere existence of acute pericarditis is not a reason for taking blood; such a measure is to be regarded only as a means of allaying the urgent symptoms of the first stage of a very acute attack.

Cold, as got by the application of an ice-bag over the region of the heart, may be of benefit at this stage. It is to be prescribed only during the acute stage. In milder cases warm poultices often give relief.

After the acute stage has been subdued, there is

generally, especially in severe cases which have required active treatment, some effusion of fluid into the pericardium. In most cases this disappears as convalescence advances and strength returns. But occasionally it is necessary to adopt measures for its removal.

Blisters repeatedly applied over the heart, and the internal administration of deobstruents, such as mercury and iodide of potassium, are the remedies usually recommended. Blisters are certainly of use; but the debilitated condition of the patient, and the weakened state of the cardiac muscles, which suffer more or less in acute cases, indicate the use of good food and tonics.

If these measures fail, and especially if the quantity of fluid be so great as to cause serious inconvenience, it may be necessary to have recourse to tapping. The trocar of an aspirator may be introduced into the distended sac without difficulty. The best point for its insertion is the fifth intercostal space, to the left of the sternum, care being taken to avoid the line of the internal mammary artery. Whether or not the operation may be ultimately successful, it always affords relief for the time. But the operation is one which is rarely called for.

In endocarditis it is very questionable if local measures ever do good. If the case is very acute, and accompanied by evidence of distress, a few leeches may be applied. But all depletory measures should

be used with extreme caution. So, too, they should in myocarditis.

There is no especial treatment applicable to myocarditis; it is essentially symptomatic. But, as a rule, the treatment of the acute stage is the same as that of endocarditis. When that stage passes off, the administration of tonics is called for. In acute cases in which there is serious impairment of the vigour of the muscular walls of the heart, stimulants should be given freely.

Attention has already been drawn to the change in the cardiac walls, induced by inflammation. They become abnormally soft and weak. It is at all times of importance that the occurrence of such a change should be recognised. It is specially so in connection with the salicyl treatment. When considering the respective merits of salicin and salicylate of soda, we saw that the latter had for one of its drawbacks a depressing action on the heart, evidenced by feebleness and, generally, increased rapidity of its action; and one or two cases were instanced to show, not only that salicylic acid produced this effect, but that no such inconvenience attended the use of salicin. In the treatment of the heart complications of acute rheumatism, it is of importance that this action of the salicylate should be borne in mind. If there is any reason to suspect the existence of inflammatory softening of the walls of the heart, the salicylate, if given at all, should have its action on the heart watched

very narrowly. If there is any evidence of the existence of myocarditis, or of feeble cardiac action, it should not be given at all ; for the addition to the already existing enfeeblement of such depression as salicylic acid may cause, would add seriously to the patient's danger. It is not in every case that salicylic acid has an enfeebling action on the heart ; but one never knows when such a case may occur. To give a remedy which may have such an action in an ailment in which cardiac enfeeblement is the special danger with which we have to deal is a practice which cannot be commended, for it cannot fail at times to produce injurious results. Fortunately it is a practice which is never called for even in the interests of the joints ; for we have in salicin a remedy which, as an anti-rheumatic, is as potent as salicylic acid, and which possesses over that acid the enormous advantage of having no depressing action on the heart.

In all cases of recent inflammation of the heart, the muscular substance is liable to be affected. In all cases in which it is affected, there is produced a soft and enfeebled condition of the ventricular walls. In all such cases the administration of salicylic acid is attended with appreciable risk : not so salicin.

Rest, quiet, good food, tonics, and stimulants in moderate quantity, are the remedial agencies to which we must trust in the treatment of this softened condition of the heart's walls.

The ailment is one which nearly always occurs in young people ; at an age, that is, at which the system possesses great recuperative powers. If not fatal in the acute stage, recovery is generally perfect. Attention has already been drawn to the fact that it may cause sudden death. The risk of such an accident would be increased by the depressing action of salicylic acid.

CHAPTER XVIII

CEREBRAL RHEUMATISM

HEAD symptoms occurring in the course of acute rheumatism are the gravest and most formidable symptoms which present themselves in that disease. There is, indeed, no malady in which delirium is of such serious import. It is so because of the grave nature of the complications of which it is symptomatic. It occurs under three conditions:—

- (1) In connection with inflammation of the membranes of the brain.
- (2) In connection with inflammation of the heart, or of its investing membrane.
- (3) In connection with hyperpyrexia.

RHEUMATIC MENINGITIS.—There are recorded a few cases of acute rheumatism in which the occurrence of marked head symptoms during life, and the presence of lymph, and even pus, on the surface of the brain after death, show that meningeal inflammation may occur in the course of that disease. But meningitis occurring in the course of acute

rheumatism is not necessarily of rheumatic origin. The extreme rarity of such cases, indeed, suggests a grave doubt whether, in the few cases in which it did occur, the meningeal mischief was not an accidental complication, due to the action of some other agency than the rheumatic poison. Certain it is that the very small proportion of cases in which such a complication occurs detracts from the interest and importance which would otherwise attach to it. Of all possible causes of head symptoms occurring in the course of acute rheumatism, inflammation of the membranes of the brain is the least likely to be the one with which, in a given case, we have to deal.

The symptoms of such inflammation would not differ from those of similar inflammation occurring independently of rheumatism. Its treatment, too, would be the same, except that appropriate anti-rheumatic remedies would be conjoined with the measures specially suited to the local head affection.

THE NERVOUS SYMPTOMS OF CARDITIS.—To the occurrence of head symptoms in connection with inflammation of the heart and its membranes, attention has already been directed; and two cases have been given in which all the symptoms during life pointed to inflammatory mischief within the cranium, but in which after death there was found nothing abnormal within the head, but only the indications of inflammation of the heart and its in-

vesting membrane. Since these cases were recorded, much attention has been given to this subject, and the observations of Bouillaud,¹ Macleod,² Hawkins,³ Bright,⁴ Burrows,⁵ Latham,⁶ Fuller,⁷ Watson,⁸ and others, have demonstrated that inflammation of the heart and pericardium is a frequent cause of head symptoms in acute rheumatism. It is chiefly in connection with pericarditis that they have been noted; this is no doubt because it is more frequent and more readily diagnosed than myocarditis. As already remarked, it is probable that the head symptoms attributed to the pericarditis are in many cases, possibly in all, indicative of a coincident myocarditis.

In studying the pathology and mode of production of these symptoms, three possible causes have to be considered :—

- (1) The morbid condition of the blood.
- (2) The cardiac inflammation.
- (3) The nervous constitution of the sufferer.

A morbid condition of the blood was the explanation on which our fathers, with the views which they held regarding the pathogenesis of acute rheumatism, naturally fell back. “A distempered condition of the

¹ Bouillaud, *Traité sur les Maladies du Cœur*.

² Macleod, *On Rheumatism*.

³ Hawkins, *Lectures on Rheumatism*.

⁴ Bright, *Medico-Chirurgical Transactions*, vol. xxii.

⁵ Burrows, *On Disorders of the Cerebral Circulation*.

⁶ Latham, *Lectures on Diseases of the Heart*.

⁷ Fuller, *On Rheumatism*.

⁸ Watson, *Practice of Medicine*.

blood I conceive to be the true proximate cause of the sensorial disturbance occasionally observed in the course of acute rheumatism.”¹ “Those remarkable cerebral affections—the wild delirium and violent mania—which not unfrequently occur in the course of rheumatic fever, or follow in its train, and which have usually manifested themselves along with the cardiac complication, causing doubt and perplexity in the mind of the physician as to the real organ affected, and the true nature of the disease, are to be explained by the morbid condition of the blood which is admitted to exist in the rheumatic constitution.”²

But this morbid condition of the blood exists in every case of rheumatic fever. If it sufficed for the production of nervous symptoms, such symptoms would be the rule and not the exception, and delirium be as common in rheumatic fever as it is in typhus. Such an explanation too rather leaves out of account the heart trouble in connection with which these symptoms are noted.

Recognising the insufficiency of this hypothesis, Sir Thomas Watson³ thought they might be due to disturbance of the cerebral circulation, resulting from embarrassment of the heart's action. The objection to this view is that the cases in which nervous symptoms are most marked are not, as a rule, those in which evidence of cardiac embarrassment occurs; but,

¹ Fuller, *op. cit.*, p. 289.

² Begbie, *Contributions to Practical Medicine*, p. 85, 1862.

³ *Practice of Medicine*.

on the contrary, those in which there are no subjective symptoms of heart disturbance, and nothing to direct special attention to that organ. The heart's action may be more embarrassed when the inflammation affects the membranes, than when it is confined to the muscular substance. But inflammation of the muscular substance causes more marked nervous symptoms. Cardiac embarrassment causes its own special symptoms, but disturbance of the nervous centres is not one of these. Such symptoms are more noted in cases of myocarditis in which there are no cardiac symptoms to attract attention (Corvisart's latent cases).

It is not unlikely that individual susceptibility may in some cases have something to do with their production. In all acute febrile ailments nervous symptoms are apt to occur. They are specially apt to do so in persons of susceptible and delicate nervous organisation. In his remarks on the case given at p. 144 Andral says: "Qu'en raison des susceptibilités individuelles, il n'est point d'organ dont la lésion ne puisse déterminer les symptômes nerveux les plus variés, de manière à produire sympathiquement les différens états morbides dont on place le siège dans les centres nerveux et leurs dépendances."

This individual susceptibility is a factor to be borne in mind in explaining the occurrence of delirium in a given case of pericarditis. But probably a more important factor is the extent to which the

muscular substance of the heart is inflamed; the occurrence of delirium in a case of pericarditis is to be regarded as evidence of accompanying myocarditis. This disturbance of nerve centres is partly due to malnutrition consequent on inefficient cardiac action, and partly, probably mainly, to the disturbance which must result from acute inflammation affecting an organ of such importance as the heart.

CHAPTER XIX

RHEUMATIC HYPERPYREXIA

EVERY now and then a case of acute rheumatism occurs which, after presenting the symptoms of the malady in the ordinary form, suddenly develops alarming nervous symptoms, with a temperature rapidly rising to 107° , 108° , 109° , or even higher, and a tendency to death by coma. Our knowledge of this condition is of recent date, and is one of the results of the more accurate clinical observation to which the use of the thermometer has led. There can be no doubt that many of the cases which our fathers described as cerebral rheumatism were cases of what we would now call hyperpyrexia.

This condition is not peculiar to acute rheumatism. It may arise in the course of any acute febrile ailment, in typhoid fever, measles, pneumonia, pyæmia, etc., or it may be a result of some lesion of the nerve centres. We find it in its simplest and plainest form as it presents itself in heat apoplexy. Indeed, the symptoms of heat apoplexy, its mode of fatal termination, and the appearances presented after death from

this cause, are exactly those which we find present themselves in hyperpyrexia as it occurs in rheumatic fever, pneumonia, typhoid fever, and other febrile diseases. Hyperpyrexia is not a disease *per se*. It is a morbid condition which may arise in the course of many ailments. It essentially consists in great rise of temperature, marked nervous symptoms, and a tendency to death by coma. Prominent nervous symptoms are as essential to its existence as the very high temperature to which it owes its name.

It has been supposed by some¹ that the high temperature of the blood causes the disturbance of the nervous centres. The objections to this view are—

First. That it gives no explanation of the occurrence of the high temperature.

Second. That the temperature of hyperpyrexia may occur, as it not unfrequently does in relapsing fever, without causing any disturbance of the nervous system.

Third. That in brain lesions it certainly is a result of the lesion.

There can be no doubt that the process is the reverse of this, and that the high temperature is a result of disturbance of nerve centres, taking rank with the nervous symptoms, and due like them to the disturbing action of some morbid agency on these centres. It is not simply an exaggeration of the

¹ Liebermeister, *Deutsch. Arch. für Klin. Med.*, vol. i., 1856.

pyrexia of ordinary febrile attacks, but a morbid condition implanted on the pre-existing fever. How is it brought about?

The thermal apparatus of the body consists:—

- (1) of the tissues in which heat is formed;
- (2) of the surface from which heat is eliminated;
- (3) of a central controlling power in the nervous

centres;

(4) of nerves connecting this with the heat-forming parts of the body;

(5) of nerves connecting it with the heat-eliminating surface.

The harmonious working of these different parts of the thermal apparatus gives rise to the phenomena of thermogenesis; and the general result is a persistent temperature of 98.4° . Interruption of this harmony causes the temperature to rise or fall. Fall of temperature is due either to lessened formation or increased elimination of heat. Rise of temperature is produced either by increased formation or decreased elimination.

Rise of temperature due to direct stimulation of the process by which heat is formed must be brought about by an agency which increases tissue metabolism. Heat is an excretory product, a result of retrograde tissue change, and cannot be produced apart from that change. It is not possible that heat could be directly brought about by stimulation of a heat-producing centre, without increased tissue change.

Increased heat due to direct stimulation of the heat-producing process must be due to the operation of some agency capable of causing increased activity of tissue metabolism. We can no more have increased formation of heat without increased activity of the processes during which heat is formed, than we can have increased formation of urea or increased formation of carbonic acid without increased activity of the processes during which they are formed. That the continuance of normal tissue metabolism is dependent on influences conveyed to the tissues by the trophic nerves is undoubted. And it is quite conceivable that stimulation applied to the centres whence these trophic nerves proceed, might, by causing increased activity of tissue metabolism, give rise to increased production of heat. The experiments of Messrs. Aronsohn and Sachs,¹ in which electrical stimulation of a particular portion of the corpus striatum produced a rise of temperature varying from $2\frac{1}{2}$ to $4\frac{1}{2}$ degrees Fahrenheit, would seem to indicate that fever may be produced by direct stimulation of a certain portion of the nervous centres; and the possibility of such a result must be kept before us in investigating the mode of production of the febrile phenomena of any given disease. But equally must it be borne in mind that such a result could be brought about only by causing increased activity of the metabolic changes by

¹ "Die Beziehungen des Gehirns zur Körperwärme und zum Fieber," *Pflügers Archiv*, Bd. xxxvii., October 1885.

which heat is formed in the tissues. Such a nerve centre is only one portion of the heat-producing apparatus, and it is quite possible that stimulation applied to other parts of this apparatus might cause the temperature to rise without primary stimulation of a nervous centre.

Besides dominating heat production the nervous centres control heat inhibition, and by so doing keep the temperature at the normal standard in health ; and in disease prevent it from passing due bounds.

Inhibition restrains and regulates functional activity as the reins restrain and regulate the pace of a spirited horse. Slacken the reins, and he hastens his pace ; let them go, and he is off at the gallop. Inhibition is an active not a passive agency, and is in constant operation. This is well exemplified by the action of the vagus on the heart ; stimulation of that nerve slows the heart's action, and, if the stimulus be strong enough, may arrest it altogether, the arrest taking place in diastole. But the nervous system which supplies this inhibiting force supplies also another, which, reaching the heart by another channel, has exactly the opposite effect ; it stimulates the heart to increased activity. These two forces are in constant operation, and so counterbalance each other that the heart is normally kept beating at the rate of about seventy a minute.

There is no organ whose normal amount of work represents the full measure of its capacity ; there is

no function whose normal state of activity represents the full possibilities of its performance. Each is restrained and kept within physiological bounds by the inhibiting action of the nervous system. Tissue metabolism is no exception to the rule. Normally, tissue formation and tissue disintegration counter-balance each other. But let the reins be slackened, let inhibition of metabolism be impaired, metabolism is necessarily increased, and pyrexia results. Let the reins be cast loose, let inhibition be paralysed, and metabolism, freed from control, is off at the gallop, and hyperpyrexia results. Hyperpyrexia may be defined as paralysis of inhibition of metabolism; paralysis of heat inhibition being only part of the process.

The clearest and most undoubted cases of rise of temperature resulting from paralysis of heat inhibition are those in which such rise occurs as a result of a lesion of nerve centres—cerebral tumour, cerebral hæmorrhage, or injury to the cervical portion of the cord.

It is impossible to regard the results of such lesions, consisting as they essentially do of pressure upon, or laceration of, a portion of the nervous centres, as other than paralytic in nature. The effect of all such mechanical lesions is not to increase, but to impair or abolish function—to produce more or less paralysis. The only way in which a destructive and non-inflammatory lesion could cause temperature to rise is by impairing

that function which normally prevents it from rising—in other words, by impairing heat inhibition. Rise of temperature thus produced will vary according to the extent of the lesion; in slighter injuries there may be no serious damage to the nervous centres, and no greater rise of temperature than is noted in cases of cerebral hæmorrhage in which the sanguineous effusion is small and does not open into the ventricles. In more extensive lesions, in which these centres are more seriously damaged (as in severe cases of cerebral hæmorrhage in which the effusion is more extensive and tears its way into the ventricles), the temperature rises rapidly and to a much higher point; while the highest temperature of all is noted in cases of crushing of the cord, in which the heat-forming parts of the body may have their connection with the heat-inhibiting centres cut off more completely than is likely to be the case in any intracranial lesion.

Admitting that the nervous system possesses the power to control and limit heat formation and prevent undue rise of temperature, we have no difficulty in the maladies and injuries to which reference has been made, in attributing the increased body heat to interference with that function. The temperature rises because the reins are slackened. The sequence of events seems to admit of no other explanation. Carrying on this line of argument,

we cannot fail to see, not only that the rise of temperature thus induced must be directly as the extent to which heat inhibition is impaired, but that paralysis of this function, by abolishing inhibition and leaving heat production in uncontrolled possession of the field, must lead to hyperpyrexia. And the more we consider the pathogenesis of febrile heat, the more apparent does it become that impairment of inhibition is a much more likely cause of hyperpyrexia than is direct stimulation of heat production. Heat inhibition remaining unimpaired, tissue metabolism could not cause those very high temperatures which characterise some cases of hyperpyrexia. Heat inhibition being paralysed, the temperature cannot fail to rise, and to rise rapidly, so long as tissue metabolism and heat production continue.

All cases of hyperpyrexia we, therefore, regard as of neurotic origin—as due to some cause which exercises a paralysing influence on the heat-inhibiting function. Pyrexia may result either from increased production or from defective inhibition, but hyperpyrexia is due only to defective inhibition.

In the cases instanced there has been a direct lesion of the nervous centres to explain the paralysis of inhibition. Other cases there are in which hyperpyrexia is as marked, but in which the sequence of events by which it is brought about is not so apparent. Rheumatic hyperpyrexia is a case in

point. Another is heat apoplexy; and it will lead to a clearer understanding of the whole subject if we premise what we have to say regarding rheumatic hyperpyrexia by a brief consideration of the process by which heat apoplexy is brought about.

That continued exposure to a high temperature is likely, in a native of a temperate climate unaccustomed to such exposure, to cause disturbance of the thermal apparatus there can be no doubt. Heat is an excretory product requiring to be eliminated; its chief seat of formation is the muscles; its main channel of elimination is the skin; a high temperature of the atmosphere necessarily interferes with such elimination, because in such an atmosphere heat cannot readily be thrown off. Heat elimination being thus checked, and heat production continuing as usual, heat must accumulate in the system, unless some agency steps in either to increase elimination or diminish formation. Under ordinary circumstances nature provides the remedy; for the same atmosphere which makes heat elimination difficult, causes also increased activity of the skin, and so meets the difficulty which itself creates; while the general influence of residence in a hot climate leads to habits of life which diminish tissue metabolism and heat production; thus the risk of heat accumulation is diminished at both ends. But circumstances every now and then arise which break through these habits. Such circumstances are those

which call for exposure and muscular effort during the heat of the day, as in the case of soldiers on the march. Tissue metabolism and heat production are stimulated, while the body is exposed to a temperature which makes a corresponding increase in heat elimination difficult. Nature guards against this danger by restraining heat production. This she does by increased activity of the heat inhibiting function.

The difficulty in the present case is the throwing off of the heat in consequence of the high temperature of the surrounding atmosphere. This difficulty only creates a necessity for more vigorous effort on the part of the heat-inhibiting centre; this centre, therefore, continues to work at high pressure, and struggles to keep the temperature down till over-stimulation leads to exhaustion; the struggle is too much for it; its efforts become feebler; it gets more and more unfit to cope with the difficulty; and ultimately, overcome by fatigue, it ceases to act. Thus is removed the last safeguard; heat production goes on apace, heat rapidly accumulates in the system, and heat apoplexy with its attendant hyperpyrexia results. What takes place in the thermic centre in such circumstances is the counterpart of what takes place in the respiratory centre when an excess of carbonic acid in the atmosphere, by the ordinary laws of diffusion, prevents the due elimination of that gas from the blood. The first effect of an increase of carbonic acid in the blood is to

stimulate the respiratory centre and cause increased force and frequency of the respiration. If the amount of gas in the atmosphere be so great as to make its due elimination impossible, that gas accumulates more and more in the blood; the respiratory centre gets fatigued, its efforts become feebler, the respirations becomes slower, the interval between them longer, and finally they cease. The cause of their cessation is paralysis of the respiratory centre induced by over-stimulation and fatigue; and the cause of this is not the inhalation of carbonic acid from without, but the impossibility of eliminating in an atmosphere of that gas the carbonic acid which is formed in the system. So in heat apoplexy it is not the heat of the surrounding atmosphere which raises the temperature of the body; it is the accumulation in the body of the heat formed in the tissues, and which is with difficulty eliminated in a hot atmosphere; it tends to accumulate in the blood, and the only way to prevent disaster is to limit heat production. With this object the heat-inhibiting centre is stimulated to make unusual efforts. In many cases it succeeds, and the only evidence of the struggle is very free perspiration and a sense of exhaustion. But the struggle may be too much for the inhibiting centre; it gets fatigued; its efforts become feebler; heat production goes on apace; heat inhibition is in abeyance; the reins are cast loose, and hyperpyrexia results. Thus is explained the hyperpyrexia of heat apoplexy.

Rheumatic hyperpyrexia might be merely an exaggeration of the ordinary pyrexia of rheumatic fever; or it might result from a direct paralysing action of the rheumatic poison on the heat-inhibiting centre; or it might be produced in the same way as heat apoplexy by over-stimulation and consequent paresis of that centre.

The first hypothesis is scarcely adequate, for were the hyperpyrexia of rheumatic fever merely an exaggeration of the ordinary pyrexia of the disease, cases in which it occurs would be characterised by inordinate severity of the rheumatic symptoms. But such is not the case. In cases which become hyperpyretic the disease up to the onset of the hyperpyrexia may present no unusual features. The temperature, the joint pains, the acid sweats, the heart complications, may all be such as are met with daily in ordinary rheumatic attacks; and there may be nothing in their symptoms to lead the physician to anticipate so alarming a complication.

The hypothesis that it may result from paralysis of the heat-inhibiting centre consequent on the direct toxic action on that centre of the rheumatic poison, or some product of the rheumatic process, is one regarding which no more can be said than that it is possible. Against it may be adduced the argument that were such the mode of production of rheumatic hyperpyrexia, that condition would arise more frequently than it does. The rheumatic poison and the

products of the rheumatic process operate in every case, but rheumatic hyperpyrexia is of comparatively rare occurrence. Then, again, hyperpyrexia occurs in other fevers and other morbid states in which the rheumatic poison does not operate.

The third hypothesis is one for which more may be said, for between heat apoplexy and rheumatic hyperpyrexia there are many points of analogy. The symptoms and clinical features of both are very much alike, and the description of the *post-mortem* appearances observed in the one serves equally to describe those noted in the other. Treatment, too, is the same in both. The main difference between them is in the circumstances which lead up to their occurrence. With so many points of resemblance between them we cannot but look for a common mode of production, some common pathological bond. The question for consideration is the possibility of the rheumatic process, as it exists in acute rheumatism, producing the same result as we find follow exposure to great heat. This latter acts by over-stimulating, fatiguing, and finally paralysing the thermic inhibitory centre. The question before us, therefore, narrows itself into a consideration of the point as to whether or not over-stimulation and consequent fatigue of the heat-inhibiting centre is a possible result of the process of acute rheumatism. Wide as is the difference between that process and great heat, and great as seems the improbability of two such different agencies producing

the same effect on the system, a careful consideration of the facts nevertheless leads to the conclusion that such result is not impossible. Certain it is that if over-stimulation and fatigue of the heat-inhibiting centre and consequent impairment of heat inhibition could be a result of any fever, rheumatic fever is the one in which it would most likely occur, and that for the following reasons :—

In all fevers the rise of temperature results from increased tissue metamorphosis. This is the case, in rheumatic fever, as it is in typhus, typhoid, and other fevers. But the circumstances under which that increased metabolism takes place in rheumatic fever are altogether peculiar; and the peculiarity of these circumstances it is which leads up to the phenomenon which we are now considering—the greater tendency to the occurrence of hyperpyrexia.

Rheumatism is essentially a disease of the motor apparatus of the body. Part of this motor apparatus—the muscles—is the chief seat of heat production. The more active the metabolism of the muscles, the greater the amount of potential energy produced. This potential energy may take the form of work or of heat. As a matter of fact, it generally assumes the form of work, for it is when muscles are actively contracting that this potential energy is chiefly formed. But if the same metabolic changes which take place in a contracting muscle were to take place in that muscle when quiescent, the potential energy

would take the form not of work but of heat. This is what occurs in acute rheumatism. The rheumatic poison causes general febrile disturbance accompanied by inflammation of the muscles and fibrous textures of the large joints. Inflammation of these textures is of course accompanied by increased flow of blood to, and increased metamorphosis in, them.

That such increased metabolism as occurs in muscle during work occurs also during the course of rheumatic fever, is demonstrated by one of the essential phenomena of that disease—increased formation of lactic acid; and the very large extent to which this acid is formed is indicative of the very large increase of the muscle metabolism to which it owes its formation. Rheumatic fever is the only form of fever in which this occurs, because it is the only one whose poison finds its nidus in muscle. The propagation of this poison in muscle gives rise there to the same increased metabolism which would result from natural stimulation.

Muscle being the chief seat of the formation of heat, and the metabolism of muscle being the chief source of heat, it follows that the disease in which such metabolism is most active is also that in which most heat will be formed. That disease is acute rheumatism. Theoretically, there is thus reason to believe that heat production is more active in acute rheumatism than in any other disease. There is also practical evidence that such is the case. The natural

result of increased formation of heat is its increased elimination. The skin is the channel by which heat is eliminated. Profuse perspiration, the evidence of excessive action of the skin, forms one of the characteristic features of rheumatic fever. Excessive production is thus met by excessive elimination of heat, and no undue rise of temperature occurs.

But another result of such increased activity of the heat-producing process must be stimulation of heat inhibition. The function of the heat-inhibiting centre is to restrain excessive formation of heat—excessive formation of heat, though common to all fevers, is most marked in acute rheumatism; that function is, therefore, likely to be called into more active operation in acute rheumatism than in any other disease. It might happen, either from want of vigour, or from unusual susceptibility of nerve centres, aided possibly by more or less failure in the heat-eliminating action of the skin, that heat production was in excess of heat elimination. Under such circumstances heat would accumulate in the system. As a result of this the heat-inhibiting centre would be first stimulated to excessive effort, then fatigued, and finally paralysed, as in heat apoplexy, and hyperpyrexia would result. That is a sequence of events which might occur in any form of fever or in any ailment accompanied by increased activity of the heat-producing process. The more active that process the more likely is it to happen. Acute rheumatism being the ailment in

which heat is most abundantly and rapidly formed, is also the one in which inhibition is most likely to be overmatched. Hyperpyrexia is, therefore, more common in it than in any other form of fever.

Though for convenience' sake we refer to paralysis of heat inhibition as the immediate cause of the very high temperature, it is evident that it is not only heat inhibition, but inhibition of metabolism in general that is paralysed. It is not the high temperature that causes the nervous symptoms, but disturbance of an important part of the nervous centres that causes the high temperature. In accordance with this we find that, both in heat apoplexy and in rheumatic hyperpyrexia, the occurrence of the high temperature is generally preceded by headache, giddiness, restlessness, or other indication of disturbance of the nervous centres. All Indian authorities refer to these premonitory indications in the case of heat apoplexy. In cases of acute rheumatism which become hyperpyretic, evidence of disturbance of the nervous system often precedes the hyperpyrexia; such disturbance should put us on the watch for graver symptoms.

Hyperpyrexia as it occurs in rheumatic fever is not a part of the rheumatic process, but an accidental complication. It is not due, like the joint inflammation and heart complications, to the direct action of the rheumatic poison, and is not to be treated in the same way. For this reason the salicyl compounds, though they put a stop to the rheumatic process,

have no controlling influence in rheumatic hyperpyrexia.

Hyperpyrexia essentially consists in paralysis of inhibition of metabolism. Such paralysis may result either from organic lesion or functional disturbance of the nervous centres. The very high temperature to which the condition owes its name is the special indication that the function of heat inhibition is impaired; just as the very rapid pulse (150 to 160) and the very frequent and hurried respiration indicate that inhibition of the cardiac and respiratory functions is so too. When hyperpyrexia is due to organic lesion, treatment is of no avail. When due to functional disorder, as is the case in rheumatic hyperpyrexia, it may be cured. In the treatment of this condition the external application of cold is the remedy on which we chiefly depend. How does the cold act? The opinion generally held is that the cold allays the disturbance by lowering the temperature. But to say that mere lowering of the body heat is sufficient to allay the alarming symptoms is equivalent to saying that these symptoms are caused by the high temperature, and that we have seen is not the case. In hyperpyrexia the external application of cold not only lowers the temperature, but arrests the whole morbid process and cures the patient.

The central thermal apparatus which presides over heat formation, heat inhibition, and heat elimination, is necessarily in free communication with the skin;

for it is in the skin that sensations of heat and cold are felt, and it is through the skin that heat is eliminated. The superficial nerves which receive the impressions of heat and cold must be connected with the centres in which these sensations are registered, and such centres must be associated with the function of heat inhibition. It is on the extremities of these nerves that the cold acts, and it is along these nerves that this peripheral excitation is transmitted to the inhibiting centres; the action is essentially a stimulant one; but to stimulate inhibition is the physiological and scientific method of allaying undue functional activity. Just as heat (as in heat apoplexy) paralyses inhibition and thus causes the temperature rapidly to rise, so cold stimulates inhibition and thus causes this abnormal temperature to fall. Just as it is not the direct heating up of the body by the hot atmosphere that causes the very high temperature of heat apoplexy, so it is not the direct cooling action of cold on the body that cures this condition. The heat acts by impairing, maybe even paralysing, the function of inhibition; the cold acts by stimulating that function into renewed activity. Its action in this respect may be compared with, and illustrated by, the action of digitalis in some forms of heart disease. When we find the heart acting in an unnecessarily disturbed and excited manner, as it frequently does in mitral disease, we do not combat this condition by efforts to soothe the excito-motor nerve of the heart; no, we

rather gain our object indirectly by giving digitalis and stimulating to increased activity the counterbalancing force—the cardiac inhibitory nerve—the vagus. In doing so we adopt a line of treatment which is not only found in practice to be the most successful, but is also the most scientific, and that which is most in accord with the teachings of physiology and the operations of nature.

In hyperpyrexia treatment must be prompt and vigorous. Inhibition, one of the most important functions of organic life—one which is absolutely essential to the continuance of life—is all but paralysed. The remedy is the application in full dose of that which stimulates it into increased activity—the external application of cold. Ice to the surface, pouring cold water over the body, wrapping it in a cold pack, putting it in a cold bath, are the active means by which inhibition is stimulated and the hyperpyretic condition subdued in urgent cases. In cases in which the danger is less urgent a tepid bath or tepid sponging may suffice ; but in all the principle is the same, the application to the surface of the body of water having a much lower temperature than the body. Where the temperature is very high and the danger very urgent, rubbing the body with ice or putting it in a cold bath till the temperature falls to 100° is the most speedy means of attaining the desired end, care being taken not to cause too great dépression. Where the danger is less urgent the

desired end is sufficiently attained by keeping ice applied to the head, and by, at the same time, frequently sponging the body with cold or tepid water. A simple and efficacious plan is to keep flipping the surface of the body, now the chest and abdomen, now the back, and now the limbs, with a sponge slightly moistened with cold or tepid water; the sponge should be soft, of loose texture, not more than two inches thick, and four to six inches in diameter. A sponge of that sort is easily flopped lightly and rapidly up and down on the surface; the fanning action by which this is done aids the action of the cold water in producing the stimulant action on the peripheral extremities of the nerves by which the desired impression is conveyed to the heat-inhibiting centre; it tends also to promote heat elimination.

The practice of treating fever by cold baths is an old one which had fallen into disuse. The good results got from this treatment in hyperpyrexia led to its revival. If the high fever which has to be dealt with in hyperpyrexia could be thus cured, might we not also by the same agency arrest the more moderate disturbance of an ordinary pyrexia? Such was the train of thought. Natural enough, but founded on a fallacy. It assumes that the two morbid conditions are similar in nature, and that hyperpyrexia is an exaggeration of pyrexia. But they are essentially different in their mode of production; hyperpyrexia is of neurotic origin, dependent on impaired inhibition,

while pyrexia (that of idiopathic fever at least, which is the form of fever chiefly dealt with) is of metabolic origin, dependent on increased production of heat. Its curing hyperpyrexia is no proof that cold can cure pyrexia. And experience shows that it does not; for though some German physicians tried to show that the course of typhoid fever may be arrested by the cold bath, their results have not been confirmed or accepted by subsequent observers.

Judiciously used, however, cold is a valuable agent in the treatment of fever; for though it may not cure it tends to alleviate some of the symptoms, especially those referable to the nervous system. Its mode of application—in other words, the dose administered—should vary in different cases. In urgent cases of hyperpyrexia it should be given at once in full dose—that is, ice or ice-cold water should be applied to the whole surface. In cases in which fever runs high, but in which the stage of pyrexia is not exceeded,—that is to say, when the temperature ranges from 104° to 106° ,—cold sponging of the body, with ice to the head, will generally suffice. In cases in which it ranges from 102° to 104° , sponging with water from 80° to 90° F. is enough. In cases in which it does not exceed 102° , cold as an antipyretic is not called for, but tepid sponging is grateful to the patient, and it is not improbable that its regular use may, by gently stimulating inhibition, prevent that function from becoming impaired, and neurotic pyrexia from being developed;

for cold produces its soothing effect less by abstracting heat than by stimulating inhibition—nature's calming agency. Cold is cumulative in its action, and should not be unduly pushed; its use should be omitted when the temperature falls below 101° , to be renewed if necessary. But it should be borne in mind that the temperature often continues to fall for some time after cold has ceased to be applied.

There can be little doubt that this most formidable complication of acute rheumatism has been of less frequent occurrence of late years. Though change of type in the disease has been suggested as a possible explanation of this, it is probable that the shortening of the duration of the disease by the salicyl treatment is the true explanation. Unlike the heart complications, hyperpyrexia does not show itself during the first few days of the illness; it may, therefore, be more readily prevented. As has already been shown, any power which the salicyl compounds may have to ward off heart complications is in many, probably the majority of, cases frustrated by the early stage at which such complications occur—the heart being affected before the system can be brought fully under the influence of the drug. Hyperpyrexia is different. It generally occurs at a later stage of the disease—not before the full action of the salicyl compounds may be got. In a case of acute rheumatism, in which this treatment is begun on the third day, the full effects of the drug are got and the disease is arrested by the

fifth day. All the complications which would have occurred after that time, had the disease been allowed to run its natural course, are necessarily prevented by the arrest of the malady. The chief and most formidable of these possible dangers is hyperpyrexia. Under these circumstances it is reasonable to suppose that the diminution in the frequency of hyperpyrexia, which has taken place of late years, is a result of the rapid cure of the disease by the salicyl compounds. Certain it is that it is since the establishment and general adoption of the salicyl treatment that hyperpyrexia has become less common.

CHAPTER XX

THE RELATION OF RHEUMATISM AND CHOREA

OF the existence of some relation between rheumatism and chorea, there can scarcely be any question. The observations of Bright,¹ Begbie,² Hughes,³ Burton Brown,⁴ Sée,⁵ Roger,⁶ and others, have placed this almost beyond doubt.

Chorea is essentially a disease of the nervous system. Its characteristic symptom is irregular and uncontrollable muscular twitching and jerking.

For the explanation of such a symptom we turn, not to that part of the nervous centres whose derangement causes delirium, wandering, and such phenomena as were noted in connection with inflammation of the heart, but to that part of them whose function it is to initiate, control, and regulate movement—the motor centres. How the rheumatic constitution leads to disturbance of these centres is the question which we have to solve.

¹ *Medico-Chirurgical Transactions*, vol. xxii.

² Begbie, *op. cit.*

³ Hughes, *Guy's Hospital Reports*, 1846.

⁴ Burton Brown, *Guy's Hospital Reports*, 1856.

⁵ *Mémoires de l'Académie de Médecine*, vol. xv., 1850.

⁶ *Archives Générales*, vol. ii., 1866, and vol. i., 1867.

There are two views on this point: one that the choreic symptoms result directly from the disturbing action on the nervous centres of the vitiated blood; the other that they are directly due to a prior affection of the heart—the rheumatic condition acting only indirectly through this.

The former view is that advocated by Begbie. “I cannot help coming to the conclusion that the simple and true view of the relation of rheumatism and chorea is to be found in the morbid condition of the blood, which is admitted to exist in the rheumatic constitution; and this explanation will apply equally to chorea occurring in individuals or families inheriting the rheumatic diathesis; to chorea occurring in connection with rheumatism, but without the cardiac complication; and to chorea associated with pericarditis, or endocarditis, or both; the inflammatory affections of the fibrous tissues, as well as the spasmodic affection of the muscles, and the derangement of the nervous system, originating in the same specific disorder of the circulating fluids.”¹ To this explanation of the choreic symptoms there is the same objection that applied to a like mode of accounting for the nervous symptoms noted in pericarditis. If due to the morbid condition of the blood, they ought to be much more common than they are; for that is a cause which operates in every case of rheumatism. Occurring, as they do, only in exceptional cases, they are more likely to

¹ Begbie, *op. cit.*, p. 84.

result from an exceptional cause, than from one which operates so generally.

The view that the chorea is consequent on a prior inflammation of the membranes of the heart, is that which has commended itself to most other observers. There is some variety of opinion, however, as to the sequence of events by which the one phenomenon leads to the other.

Bright thought that the choreic symptoms resulted from irritation transmitted from an inflamed pericardium or pleura along the phrenic nerve. This explanation might apply to cases of chorea occurring in connection with pericarditis or pleuritis, but is quite inapplicable to the numerous cases in which no such inflammation exists.

In more recent times the view has been advanced and ably advocated by Kirkes, Hughlings Jackson, Broadbent, and others, that it is to endocarditis rather than to pericarditis that we have to look for the explanation of the choreic phenomena. The theory is, that some of the particles of lymph deposited on the surface of the valves get detached, enter the circulation, and cause embolic plugging of the minute vessels of the motor ganglia; and some pathological evidence has been adduced to show that the corpora striata and optic thalami have suffered in fatal cases of chorea. The actual existence of embolism, however, has not been demonstrated; and its occurrence, as a cause of chorea, cannot be regarded as more than

hypothetical. That such an event is possible, there can be no doubt ; but if particles of fibrine are detached from the valvular surface, it is difficult to see why the vessels of other parts of the brain should not be plugged, as well as those of the motor ganglia ; and why these embolic particles should not sometimes get into other organs, and give rise to infarctions of the lung, spleen, kidney, etc.

Again, if the cause of chorea in rheumatic subjects be the detachment of particles of lymph from the surface of a roughened valve, how are we to explain its occurrence in those numerous cases in which there is no endocarditis and no roughening of the valvular surface ? To such cases this embolic theory is quite inapplicable. It cannot, therefore, be regarded as adequate. Just as Bright's theory might apply to cases of chorea occurring in connection with pericarditis, so this one might apply to cases of chorea occurring in connection with endocarditis. The fault of each is its narrowness, and the impossibility of applying it to more than a minority of the total cases of rheumatic chorea. What we want is an explanation which will apply to all cases of that disease—those occurring in connection with pericarditis—those occurring in connection with endocarditis—those occurring in connection with simple rheumatism of the joints, uncomplicated by any heart affection—and those occurring in persons of rheumatic constitution, but who, at the time of the choreic

attack, are not suffering from rheumatism of either the heart or joints.

The theories hitherto advanced have given prominence to two different factors—the morbid condition of the blood, and the inflamed condition of the heart. Neither has been sufficient to meet the whole of the facts. A much wider pathological view is required for that purpose.

Rheumatism is essentially a disease of the motor apparatus; chorea is essentially a disease of the motor centres.

In this broad pathological statement we have the clue to the explanation of the relation of the two diseases.

The motor centres affected in chorea, and the motor peripheral apparatus which suffers in rheumatism, have an essential physiological connection. The motor centres form the central portion of a system, of which the joints and muscles are the distal or peripheral. Each is essential to the physiological completeness of the other, and without the other neither has any physiological *raison d'être*. Without joints to be moved, the motor centres would be useless; without motor centres to initiate the necessary nervous force, the muscles would remain flaccid, and the joints be of no avail.

The seat of chorea and the seat of rheumatism having so close a physiological connection, it need not surprise us to find that there is some connection be-

tween these two diseases, and that chorea is more apt to occur in rheumatic than in non-rheumatic subjects.

The existence of the rheumatic diathesis implies a liability to disturbance of the motor apparatus. The motor ganglia are an essential part of this apparatus. Those subject to rheumatism are therefore, *cæteris paribus*,¹ more likely to have susceptible motor centres than those who are not. Thus the rheumatic diathesis predisposes to chorea. So much physiology teaches. But the practical questions still remain—How is the chorea induced? What is its exciting cause? and Why does it occur only in a small percentage of the total number of rheumatic subjects?

Here, as is the case with delirium and nervous symptoms generally, constitutional predisposition plays an important part. The motor centres, like all other parts of the nervous system, are more susceptible and more liable to disturbance in females than in males, and in young people than in those of more mature years. We accordingly find that it is in females and in young people that choreic symptoms are most apt to show themselves. Choreia is not a manifestation of rheumatism, and the rheumatic constitution is by no means necessary to its production. A fright, or nervous shock, gastric or uterine derangement, may give rise to chorea and be the exciting cause of the disease in persons in whom there is no history of rheumatism. But many cases there are—so many that the connection is too striking to have

escaped notice—in which a present or prior rheumatic attack, with or without heart affection, is the only cause to which the chorea can be traced. Many cases there are, too, in which a rheumatic family history forms the only noteworthy feature.

In discussing the pathology of rheumatic chorea, we thus have two different classes of cases to deal with—those in which the chorea occurs either in connection with, or subsequent to, a rheumatic attack; and those in which there is only a family history of rheumatism.

A rheumatic attack means inflammation of an essential and important part of the motor apparatus, and general disturbance of the whole system. If a nervous shock, or derangement of the digestive or uterine organs, may induce chorea in one predisposed to it, a rheumatic attack or an endocarditis may almost certainly do so too; for general rheumatic disturbance of the motor apparatus cannot but be regarded as a possible cause of disturbance of the motor centres. Thus the rheumatic diathesis may be the predisposing, and a rheumatic attack the exciting cause of an attack of chorea. The combination of these two causes in the same subject suffices to explain the special tendency of chorea to occur in those who have suffered from rheumatism. The heart complications, to which the choreic phenomena are by some ascribed, are a mere incidental accompaniment of the disease. They may, of course, act as an exciting cause in the same way as the joint affection or

derangement of the uterine organs may, but they are not essential to the production of chorea.

But the predisposing cause may exist without the exciting. There may be a family predisposition to rheumatism, without the disease having ever occurred in a given member of the family. Choreic symptoms may show themselves in such a one without any prior rheumatic attack, the exciting cause being some other disturbing agency, such as shock or gastric or uterine disturbance. No matter what the exciting cause, the disease is fitly described as one of rheumatic chorea, if what tended to its production, and predisposed to its existence, was the rheumatic constitution of the individual.

In a rheumatic subject predisposed to chorea through a susceptible condition of the motor centres, it is an accident whether the chorea, when it does occur, comes on in connection with a rheumatic attack, subsequently to it, or prior to, and independently of it. The ultimate pathological explanation of the relation of the rheumatism and the chorea is the same in each: the one disease consists in disturbance of the peripheral portion of the motor apparatus of the body; the other consists in disturbance of the motor centres.

In persons with susceptible and easily disturbed motor centres chorea may be induced by causes which would not give rise to it in others.

The motor centres are most easily disturbed in

people of rheumatic constitution, because rheumatism is essentially a disease of the parts of the body over which the motor centres preside. Other morbid conditions, gout and rheumatoid arthritis, also affect the motor apparatus without disturbing the motor centres; but then they occur at an age at which chorea does not manifest itself. Chorea is essentially a disease of youth, so is rheumatism; it is the only joint trouble which is so.

CHAPTER XXI

ANOMALOUS FORMS OF RHEUMATISM

A DEFINITE form of fever is not the only effect produced on the system by malaria.

With or without a previous attack of fever, a man exposed to malaria may lose health, become pale, listless, unfit for sustained effort, and more or less anæmic. There may be no fever, no apparent disturbance of the function of any organ. The condition has been fitly described as malarial or paludal cachexia. It is the result of the general enfeebling action of residence in a malarial district, and is not recovered from till that district is left. It is a condition of chronic malarial poisoning.

Besides this general cachexia, malaria may cause localised disturbances of particular organs or tissues. Many cases of neuritis and of neuralgia are of malarial origin; so too are certain forms of derangement of liver, spleen, and bowel. Medicinal treatment may benefit these, as it may benefit malarial cachexia, but recovery is much aided and hastened by removal from the malarial district.

The rheumatic poison likewise produces on the

system other effects besides a definite form of fever, and other local lesions than those noted in rheumatic fever. Anæmia is a sequence of acute rheumatism; indeed, there is scarcely any acute disease in which this result is produced so rapidly and to so marked an extent as it is in acute rheumatism, when the disease is allowed to run its natural course. There is too some evidence to show that children of rheumatic parentage are more apt than others to become anæmic.¹ Such a condition is fitly described as rheumatic cachexia.

The age of liability to the regular arthritic form of rheumatism, polyarthritiſ rheumatica, is from fifteen to fifty. It is within these years that rheumatism, as it commonly manifests itself, chiefly occurs. It does so because from fifteen to fifty is the period of functional activity of those textures (the fibrous structures of the large joints) which are specially affected, and because it is only during their period of functional activity that these textures are a suitable nidus for the rheumatic poison. But the rheumatic constitution does not begin at fifteen and end at fifty. It exists both before and after these limits. It is often an inheritance which exists from birth. It essentially consists in the presence somewhere in the textures of the body of a something which makes these textures a suitable nidus for the development of the rheumatic poison. From fifteen to

¹ Goodhart, *Diseases of Children*.

fifty this something exists in the muscles and fibrous textures of the large joints. Before fifteen and after fifty it exists not in the joints but in other textures, as is evidenced by the fact that the joints do not suffer. Hence it is that anomalous forms of rheumatism occur chiefly before and after the age of liability to the regular arthritic form of the disease.

It is the peculiarity of the seat of the rheumatic nidus, and the extent to which that nidus exists in the system, that determine the nature and the severity of a rheumatic attack. In ordinary rheumatic fever it exists to a large extent in the muscles and fibrous textures of the large joints; because of its existence there, the rheumatic poison is developed in, and acts on, these textures; because of its abundance the poison is developed largely, and produces a correspondingly marked inflammation.

Anomalous forms of rheumatism occur chiefly before fifteen and after fifty; but the disease manifests itself in different ways at each period. The rheumatism of childhood manifests itself by symptoms and lesions peculiar to that age. That of old age has also its own special features.

The Rheumatism of Childhood.—The textures which suffer in the rheumatism of childhood are to a great extent those which we find suffer in ordinary rheumatic fever—the motor apparatus, the fibrous textures, the heart, and the skin; only they do not suffer in quite the same way.

In connection with the motor apparatus attention has been directed in the last chapter to the frequency with which chorea, which is functional disturbance of the motor centres, occurs in children of rheumatic constitution.

The skin is much affected in rheumatic fever, acid perspirations being almost essential to the diagnosis. It has long been matter of clinical observation that various forms of erythema—erythema papulatum, erythema marginatum, and erythema nodosum—have a special association with rheumatism. Many years ago Begbie¹ drew attention to the frequent occurrence of erythema nodosum in rheumatic subjects. The following are the chief conclusions to which he came:—

“(1) The skin affection is most prevalent in, if not confined to, the young, and those under thirty, the chief subjects of the rheumatic diathesis and of rheumatic fever.

“(2) It is associated frequently with rheumatic fever coexisting or alternating with it.

“(3) It is often complicated with those internal disorders with which rheumatism is allied, particularly with pleurisy and pneumonia. It has also been noticed in connection with endocarditis, or other cardiac disease.”

More recently Dr. Stephen Mackenzie² has brought forward a mass of valuable evidence which seems amply to warrant his conclusions—

¹ Begbie, *op. cit.*, p. 104, 1862.

² *Transactions of Clinical Society of London*, vol. xix., 1886.

“(1) That erythema nodosum is frequently associated with definitely rheumatic symptoms, *e.g.* arthritis, sour sweats, sore throat, etc.

“(2) That heart disease (endocarditis) may arise during an attack of erythema nodosum, both in cases in which arthritis is present, and in cases in which there is no affection of the joints.

“(3) That these conclusions justify the inference that erythema nodosum is frequently, if not generally, an expression of rheumatism, even when no other definitely rheumatic symptoms are present.”

There can be no doubt that the rheumatic poison may in exceptional cases so affect the system as to cause pains, febrile disturbance, and maybe even acid sweats, without giving rise to any affection of the joints. Such cases usually occur in boys and girls, more often in girls. Their symptoms are slight fever, the temperature being generally about 100°, aching of the limbs, some tenderness on pressure at the seat of aching, and not uncommonly an eruption of erythema (nodosum, marginatum, or papulatum) on the arms or legs or both. The following case is given as illustrative of this condition :—A girl, aged fifteen, had always had good health, except for occasional attacks of tonsillitis. The family history is rheumatic. Her father died of heart disease at forty-five, and two brothers suffer from it now; in all the heart trouble was a sequence of acute rheumatism. On 10th May she felt out of sorts, and had pains in the back,

shoulders, and legs. On the 12th I was asked to see her because "spots" had come out on her legs and pained her a good deal. I found her with well-marked erythema nodosum on both legs, six or seven nodes on each between the knee and ankle. There was tenderness of the muscles of the shoulder and of the thighs; the tongue was furred, the pulse 84, the temperature 100.2° ; there was slight acid perspiration; there were no joint pains; the tongue was furred, and the bowels constipated. She was ordered a calomel purge, and fifteen grains of salicin every two hours; light diet, and to remain in bed.

On the following day the temperature was normal, and she felt much better. The nodules of erythema were still there, but not so red and not so painful. On the next day she had still further improved, and the nodules were bluish in colour and fading. She got rapidly well.

This case was one of subacute rheumatism in which the poison affected only the muscles and the skin. Such cases are not uncommon in girls. The fibrous structures of their large joints have not yet reached the stage of development and vigour at which they become a suitable nidus for the rheumatic poison. But the rheumatic constitution is there, and it is the muscles and skin which present the conditions necessary for the reproduction of the poison. Hence we have a rheumatic attack without any joint affection. Such cases may be fitly compared to those in

which the special lesion of the eruptive fevers is not developed—variola sine variolis, morbilli sine morbillis, typhus sine eruptione. Their rheumatic nature is demonstrated by the occasional occurrence of cases presenting exactly the same symptoms, but in which one or more joints are the seat of true rheumatic inflammation.

Sore throat (pharyngitis or tonsillitis) is common in connection with rheumatic attacks, and not unfrequently occurs in rheumatic subjects as an isolated lesion. It is most common in children.

Subcutaneous nodules form another manifestation of rheumatism in childhood, and, like other non-arthritic manifestations of that disease, are more common among girls than among boys. These nodules are round or ovoid lumps situated in some of the fasciæ or along the course of tendons. Their size varies from that of a pin-head to that of a small filbert. They may occur almost anywhere, but their most common seat is about the elbow or hand. When first they appear they may be slightly tender on pressure, but generally they are painless. They may last only a few days, or may persist for several weeks. Dr. Cheadle regards them as essentially rheumatic, and never due to any other cause. My own experience quite accords with this view. These nodules are no doubt the result of a low form of rheumatic disturbance leading to proliferation of the cellular elements and consequent increased growth of tissue at the irritated

point. They bear to the rheumatism of childhood the same relation that arthritis bears to that of adult life. What constitutes the rheumatic constitution, and makes an individual liable to have rheumatism, is the presence in the fibrous textures of the motor apparatus of something which makes them a suitable nidus for the rheumatic poison. It is when these fibrous textures have reached their full development, and in that part of them which is most highly developed and possesses most functional activity—the fibrous textures of the large joints—that this peculiar something is most abundant. It is in these textures, therefore, that the rheumatic poison is reproduced, and on them that it acts. In childhood while the fibrous textures of the joints are as yet imperfectly developed, and are not called upon to do active duty, the rheumatic poison finds its nidus rather in the fasciæ and in the tendons, and not even generally distributed through them. For this reason the rheumatic poison, when it gains entrance to the system in childhood, is apt to cause not arthritis, but inflammation of a patchy character in the fasciæ and tendons. The inflammation is not acute, and it occurs in textures of low vitality and little vascularity, in which such disturbance is not likely to spread. It is sufficient, however, to cause proliferation of the cellular elements and consequent thickening of these textures at the point of irritation. The result is the development of subcutaneous nodules.

Pleuritis and pneumonia are often of rheumatic origin, and may occur, especially pleuritis, either as an isolated lesion or in association with arthritis, erythema, or other manifestation of rheumatism. They occur both in childhood and in adult life, but more often in the young than in those of more mature years.

Endocarditis.—It has already been pointed out that in ordinary articular rheumatism heart complications are more apt to occur in young subjects than in those of more mature years, and that the younger the sufferer the greater is the danger of the heart becoming involved. It need not, therefore, surprise us to find that endocarditis and pericarditis are not uncommonly noted as occurring along with the irregular manifestations of the disease which present themselves before puberty—erythema and subcutaneous nodules. Especially in connection with the latter are heart troubles apt to arise. So grave a view does Dr. Cheadle, who has devoted much attention to the subject, take of the occurrence of these nodules that he regards “the eruption of large nodules as almost equivalent to a sentence of death. They mean persistent cardiac disease, generally uncontrollable, and marching almost infallibly to a fatal ending.”

They are unquestionably of grave import, not because of any serious effects which they themselves produce, but because they are all but invariably accompanied by progressive disease of the heart. Of

the twenty-seven cases observed and reported on by Drs. Barlow and Warner¹ all had heart disease. These nodules are, indeed, only one indication of a general rheumatic cachexia in which the fibrous textures of the heart are as apt to be affected as are the fibrous structures of the fasciæ and tendons in which these nodules occur. In acute articular rheumatism occurring before the age of twenty the heart is very often affected, and is apt to be so from the very commencement of the attack, the cardiac trouble being coincident with, if not antecedent to, the articular inflammation. In childhood we do not, as a rule, have articular inflammation, we have nodules instead. The earlier in life a rheumatic attack occurs the more likely is the heart to suffer. The heart trouble, which is an all but invariable accompaniment of these nodules, probably exists before the nodules are developed—the first incidence of the rheumatic poison being on the heart. All the structures of the heart are apt to suffer. Originating in the fibrous structure, the inflammation is apt to extend thence to the pericardium and to the muscular substance, and the younger the patient the more apt is this to happen. Hence it is that the heart troubles noted in connection with subcutaneous nodules are often more severe and fatal than those noted in connection with arthritis. It is not the nodules, but the age at which they occur, not the peculiarity of the rheumatic

¹ *Transact. Med. Congress*, 1881.

lesion, but the age of the sufferer, that makes the difference, and that causes the large mortality noted in these cases. Of Barlow's and Warner's twenty-seven cases eight proved fatal—an enormous percentage.

For this greater mortality of rheumatic inflammation of the heart in children there are two reasons : First, the organ is more excitable, beats more quickly, is therefore more affected by the disturbance which inflammation causes, and is in consequence less amenable to treatment. Rest is what is wanted ; in no case is it attainable ; but we are further from it in children than in adults, for their hearts are naturally more excitable. Second, the muscular substance is more apt to be affected in children than in adults. In the adult an endocarditis is more apt to remain an endocarditis, and a pericarditis a pericarditis ; but in early life the inflammation is more apt to spread from the fibrous structures of the rings and valves to the pericardium and to the muscular substance, producing a general carditis which at that age is with difficulty recovered from. It is this tendency to the occurrence of myocarditis which makes these cases so fatal. The heart trouble begins in the fibrous rings and valves, causing there proliferation of the cellular elements and consequent thickening. It is exactly the same change which is noted in the rheumatic endocarditis of the adult. We have already seen that in the adult the mischief is apt at times to extend to the pericardium and to the muscular substance. It is the

same in the child, only the process is a more active one, and the tendency to spread more marked.

In the child as in the adult the disease exists in varying degrees of severity. The course of acute cases is such as has been indicated. But there are many cases in which the cardiac trouble is very slight, and in which complete recovery takes place. It is not unlikely that some of the cardiac murmurs noted in some cases of chorea are really due to a temporary thickening of a portion of the fibrous textures of the heart.

The fibrous structure of the rings is proportionately more apt to be thickened in children than is the corresponding texture in the valve; hence stenosis, narrowing of the cardiac orifice, is more common as a result of rheumatism in children than it is in adults.¹

The important point to be borne in mind is that the description of the rheumatic state as it occurs in the adult does not apply to the same state as it manifests itself in childhood. In the adult, arthritis and acid sweats form the characteristic feature of the attack. In children these are replaced by erythema and subcutaneous nodules. In children, too, the heart is more liable to suffer than it is in the adult, great as is the tendency to heart trouble even there. And very commonly the first incidence of the rheumatic trouble is on the heart. In rheumatic fever the liability to

¹ It is not improbable that most of those cases of mitral stenosis in which the lesion is supposed to be congenital are really the result of rheumatic endocarditis occurring in childhood or even in infancy.

heart complications diminishes with advancing years. In other words, the younger the sufferer the more likely is the heart to be affected.

But the heart is subject to rheumatic inflammation before the joints are so. Indeed, of all the structures of the body, the fibrous structures of the heart are those which give the earliest evidence of being subject to rheumatism. To the frequent occurrence of endocarditis in connection with erythema and subcutaneous nodules reference has just been made. It often occurs independently of these, as an isolated lesion, and when it is associated with them it is probable that the endocarditis existed first. The period of greatest liability to rheumatic arthritis is from fifteen to thirty-five; the period of greatest liability to rheumatic endocarditis is from ten to twenty-five.

It is of importance that we should recognise that though acute articular rheumatism, polyarthritis rheumatica, does not usually occur before fifteen, the rheumatic tendency exists from early childhood, and that the structures which are most apt to be affected by the rheumatic poison, should it gain entrance to the system of a child of rheumatic constitution, are the fibrous structures of the heart. It is because the period of functional activity of the fibrous structures of the joints is from fifteen to fifty, that it is chiefly within these limits of age that those textures are a suitable nidus for the rheumatic poison. It is because the period of functional activity of the fibrous structures

of the heart begins so much earlier, that they earlier are a suitable nidus for the rheumatic poison, and at an earlier age become subject to rheumatism.

As there is a malarial cachexia from which some people, resident in a malarial district, are more liable to suffer from than others, so there is a rheumatic cachexia from which children of rheumatic constitution are apt to suffer without the development of joint disturbance. The evidence of its existence, the symptoms by which it declares itself, are anæmia, chorea, erythema, subcutaneous nodules, endocarditis, pericarditis, myocarditis, pleuritis, one or two or more of these. The gravity of the condition depends much on the extent to which the heart is affected. Unfortunately that organ is in not a few cases hopelessly damaged before the patient comes under notice.

The treatment of these anomalous forms of rheumatism is not different from that which should be adopted in the arthritic form of the disease. The tendency to heart complication is so great that salicylate of soda should be used with great caution. Salicin given in frequent dose, and some alkali, are the suitable remedies. Absolute rest in bed, and light nourishing diet, are important till one is confident that the danger to the heart is surmounted.

Hyperpyrexia does not occur in the rheumatism of childhood. The muscles and heat-forming apparatus are not so disturbed as in the more acute rheumatic attacks of the adult. Heat inhibition is not stimu-

lated so as to keep down excessive formation ; there is, therefore, no chance of this function being exhausted or paralysed. The circumstances which combine to produce such a result in the adult do not exist in the child.

In advanced life rheumatism assumes an anomalous form, inasmuch as it does not take the form of arthritis.

The structures which chiefly suffer are the large muscles, their aponeurotic attachments, their sheaths, and their tendons. The larger nerves and their sheaths, especially the brachial plexus and the sciatic—the nerves, that is, which supply the chief structures affected in articular rheumatism—are often the seat of a low form of rheumatic disturbance. Rheumatism affecting these structures is never acute in character, and does not give rise to fever. The pain is generally dull and aching, and is increased by movement and by pressure over its seat.

Just as the special rheumatic manifestations of childhood may also occur in early adult life, so these more senile manifestations of the disease may occur in middle life, especially in women. They are most common, however, after fifty. At whatever time they occur they are apt to be obstinate.

The chief remedies are salicin, salicylate of soda, quinine, and iodide of potass. With this general treatment there may often fitly be combined massage, rubbing, and such treatment as is got at Bath, Buxton, Harrogate, Strathpeffer, and at various baths in France and Germany.

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